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ACADEMICIAN VLADIMIR MIKHAILOVICH RODIONOV

(On his 75th Birthday Anniversary)

M. M. Shemyakin

On October 28, 1953, the 75th birthday anniversary and the 50th anniversary of the scientific, practical and pedagogical activities of one of the most outstanding Soviet chemists – Academician Vladimir Mikhailovich Rodionov – was celebrated.

V. M. Rodionov belongs to those men who are exceptionally endowed and gifted by nature. His personality is a brilliant combination of scientist, engineer, pedagog and social worker.

The theoretical works of V. M. Rodionov and his school bear the marks of profound scope of investigation and variety of problems studied. Within the 50-year period of his scientific activity, V. M. Rodionov has extended his investigations in the organic chemical field to such diverse types as aliphatic, alicyclic, aromatic and heterocyclic series, relative to dyes, alkaloids, pharmaceuticals, vitamins and perfumes. In particular, V. M. introduced much that is new, valuable and original into the field of β-amino acids, into pyrimidine and imidazole chemistry and other heterocyclic compounds, as well as the chemistry of aromatic compounds, in particular, of aldocarboxylic acids. Discovered and developed in detail were successful procedures for the alkylation of organic compounds, an original method for introducing the diazo group into phenols, quite ingenious in its simplicity of method, methods of synthesizing β-amino acids and their analogues, and procedures for converting β-amino acids and their derivatives into various types of heterocyclic compounds, which are widely known. Of excellent caliber was V. M.'s investigation on the mechanism of the Hofmann degradation of carboxylic acid amides. Of added interest are the possibilities opened up by V. M. for utilization of this reaction for synthetic purposes, in particular, for the derivation of certain types of heterocyclic compounds. The fundamental investigations of V. M. in β-amino acid chemistry, carried out in 1946, were honored by the 1st order Stalin prize. The extensive works of V. M. in the chemistry and technology of organic intermediates and dyes, which have been extensively applied in the industry, were also honored by the Stalin prize in 1949 and in 1950. V. M. Rodionov has assembled many students and co-workers, and has created a large school, the labors of which are a valuable heritage of science and technology. He has published about 180 works on various problems of chemistry, technology and economics, has published a series of interesting reviews, and has written many articles on the works and life activities of prominent Russian and Soviet scientists.

Being both an researcher and an engineer at the same time, and having always been closely related to various branches of the chemical industry, V. M. Rodionov in his active period has invariably aimed at combining his theoretical research with the practical needs of socialist development. A number of his works in the fields of alkaloids, pharmaceuticals, organics, intermediates, dyes and aromatic substances were directed toward solutions of actual problems of immediate interest to industry, and many developed methods for synthesizing organic compounds were put into production by his direct participation. V. M. Rodionov is one of the founders and first leaders of the national aniline dye and pharmaceutical industries. At the present time he continues to take an active part in development of the chemical industry, having been for many years assistant to the Chairman of the Technical Soviet Ministry of Chemical Industry, visiting plants, consulting with industrial workers, and carrying out with them a number of joint investigations. Recently, V. M. has given particular attention to development of the synthetic aromatic industry.

The social and scientific-organizational activities of V. M. Rodionov are also quite versatile. For many years he has actively participated in work of the D. I. Mendeleev All-Union Chemical Society, being first chairman of the section, then vice-president, and finally president of the society. He has also devoted considerable attention to scientific-organizational work in the Academy of Sciences of the USSR. V. M. participates actively in various scientific and technical conferences, delivering reports and in discussions. It is sufficient to mention that within the past few years he has participated in numerous conferences held in Moscow, Leningrad, Kiev,

Erevan, Tashkent, Irkutsk, Kuznetsk and other cities. V. M. is an editor and member of the editorial boards of several scientific journals and scientific-technical publications. For many years he has been a member of the Expert Commission on Chemistry of the VAK (Ministry of Culture). All who are acquainted with V. M. Rodionov hold him in great esteem, praising him highly for his exceptional knowledge and experience, his principles and his inexhaustible initiative and energy.

We should linger upon one more side of V. M. Rodionov's activities – his pedagogical work, which began at the Moscow Higher Technical School, and which has continued uninterrupted up to the present time at various institutions of higher learning in Moscow. At first he gave lecture courses in pharmaceutical chemistry and the chemistry of alkaloids, which were synthesized in an interesting manner, and later he lectured in courses on the chemistry and chemical technology of dyes and intermediates, and for the past decade and a half – courses in organic chemistry. V. M.'s lectures are simple and clear in outline, always of profound subject matter, and interesting; in them he propounds not only the bases of theoretical concepts, but also the principal veins of creative thought by investigators, and reflects upon all of the important achievements of science and technology, imparting to them his large, accumulated experience in scientific and practical matters. V. M. always devotes much of his attention and powers to leadership of the scientific work of the undergraduate and graduate students, and of his numerous co-workers Of exceptional erudition, and being possessed of an excellent memory, being interested, and following continuously developments in various branches of chemistry and chemical technology, as well as being, himself, an excellent experimenter, V. M. is found to be an outstanding leader and teacher for young, scientific workers. He behaves as an elder colleague with both co-workers and students alike. He knows how to discover and to develop able students, giving them always the opportunity to develop their abilities. With his authority he does not suppress the initiative of young scientific workers, but helps them through advice and by sharing experiences with them, which unquestionably contributes to their growth and to their emergence into the scientific field. V. M. Rodionov has educated hundreds of engineers and investigators who, at the present time, occupy leading positions in industry, in institutions of higher learning, and in research institutes. Many of his pupils have already created their own scientific approaches and schools.

V. M. Rodionov is not only a great scientist, but also a charming and sensitive man. All who have met him in their lifetime know well his kindness and responsiveness, his affability and directness in dealing with people. From the first moments of being in his company, all feel entirely at ease, as though they had known him for many years, and feel a kinship with him. One can approach him with any problem and he is always ready to respond, will try to help with advice and action whether the problem is scientific or personal. Nonetheless, as a man of high principles, and considering honesty in people and in himself above all, V. M. with all of his charm can, when necessary, be severe and rigid. However, he usually establishes friendly relationships with his pupils and co-workers for many years. V. M. displays lively interest in their works and takes sincere pleasure in their creative success and achievements in science. V. M. loves his science deeply and knows how to inject into his pupils an objective love for it.

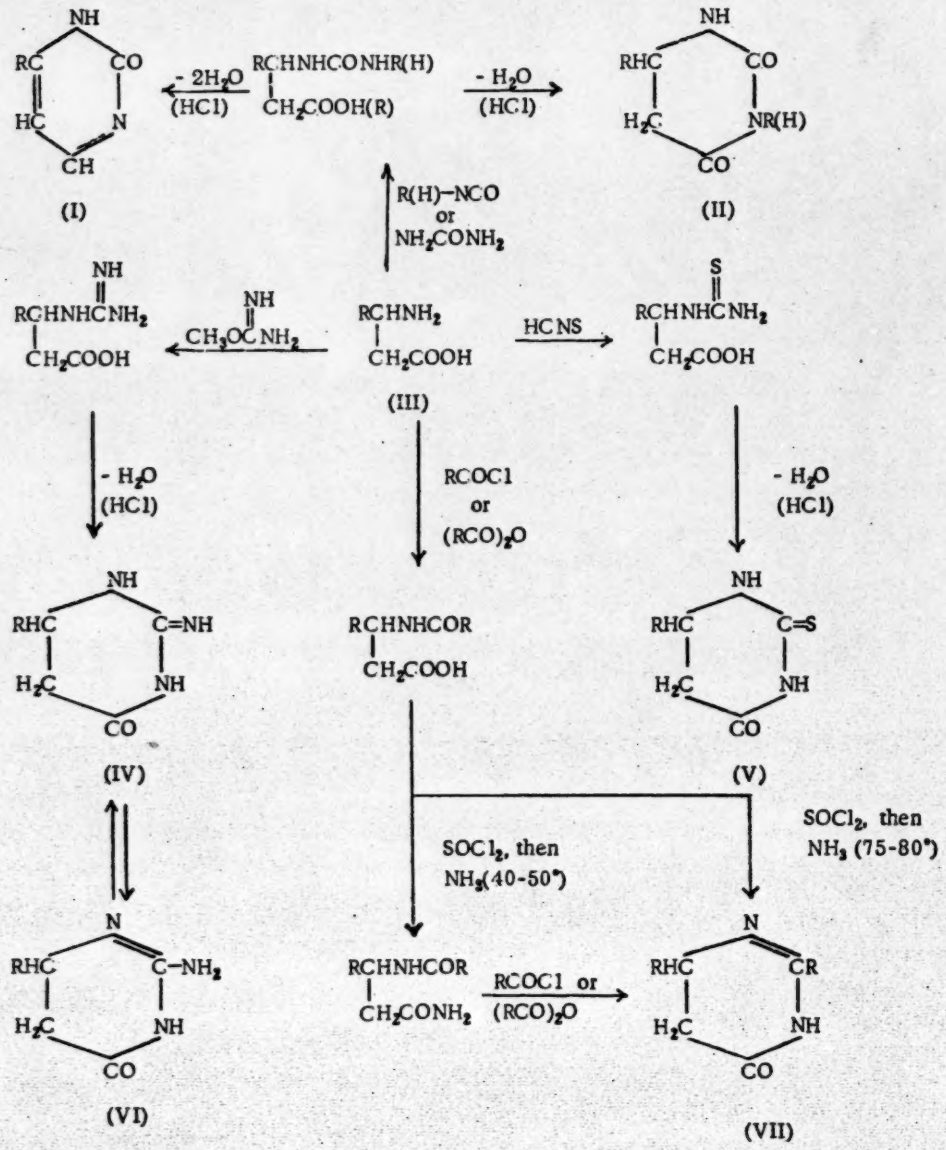
When speaking of V. M. Rodionov, there should not be forgotten another rare and valuable characteristic. The brilliance of his thought, the keenness of his mind, the inexhaustible love of scientific creation, the diversity of his interests – all of this remains unchanged and forces us to forget his age. Lately V. M. Rodionov has expanded his investigations on a particularly broad scale of most diverse fields; within the past 5 years, he has published about 70 articles on various organic chemistry problems which are of considerable theoretical and practical interest. This research requires more detailed illustration.

As in preceding years, V. M. Rodionov, together with a number of his pupils and co-workers (V. G. Avramenko, L. V. Antik, N. N. Bezinger, T. K. Veselovskaya, V. K. Zvorykina, V. V. Kiseleva, T. S. Kiseleva, N. A. Kravchenko, B. I. Kurtev, O. S. Urbanskaya, A. M. Fedorova, E. I. Chukhina, E. V. Yavorskaya, N. G. Yartseva and others), has paid particular attention to β-amino acid chemistry, and in particular, to methods for their conversion to various types of heterocyclic compounds [1-22]. All of these investigations of V. M. have created considerable interest, particularly since certain β-amino acids, as well as heterocyclic compounds resulting from them, enter into the composition of many biologically-active natural and synthetic compounds – antibiotics, vitamins, nucleic acids, pharmaceutical preparations, and others.

During the period 1948-1953, V. M. Rodionov has extended considerably the field of application of the method which he discovered in 1926 for synthesizing β-amino acids; synthesis of a number of new β-amino acids and their various derivatives has been realized by this method, the effects of structural and external factors during the course of their formation have been studied, the validity of the reaction mechanism earlier proposed has been confirmed, and optimal conditions for carrying out the reaction have been worked out. At the present time, the V. M. Rodionov method has become the most popular, and no doubt best, procedure for synthesizing various β-amino acids, their derivatives, and analogs. synthetic yields of which, in many cases, have reached as high as 70%.

In continuing means of investigating β-amino acid conversions into various heterocyclic compounds, V. M. has recently also studied in a number of cases the possibility of transition from β-amino acids (III) to substituted di-, tetra- and hexahydropyrimidines of the type (I), (II) and (VII), observed earlier by him, and at the same time has developed new synthetic procedures for substituted hexahydropyrimidines of types (V) and (IV) ⇌ (VI) (see scheme 1). A thorough study of the conditions of these reaction processes made it possible finally for V. M. to develop very simple, and in many cases general, methods for synthesis of substituted pyrimidines of the type enumerated above.

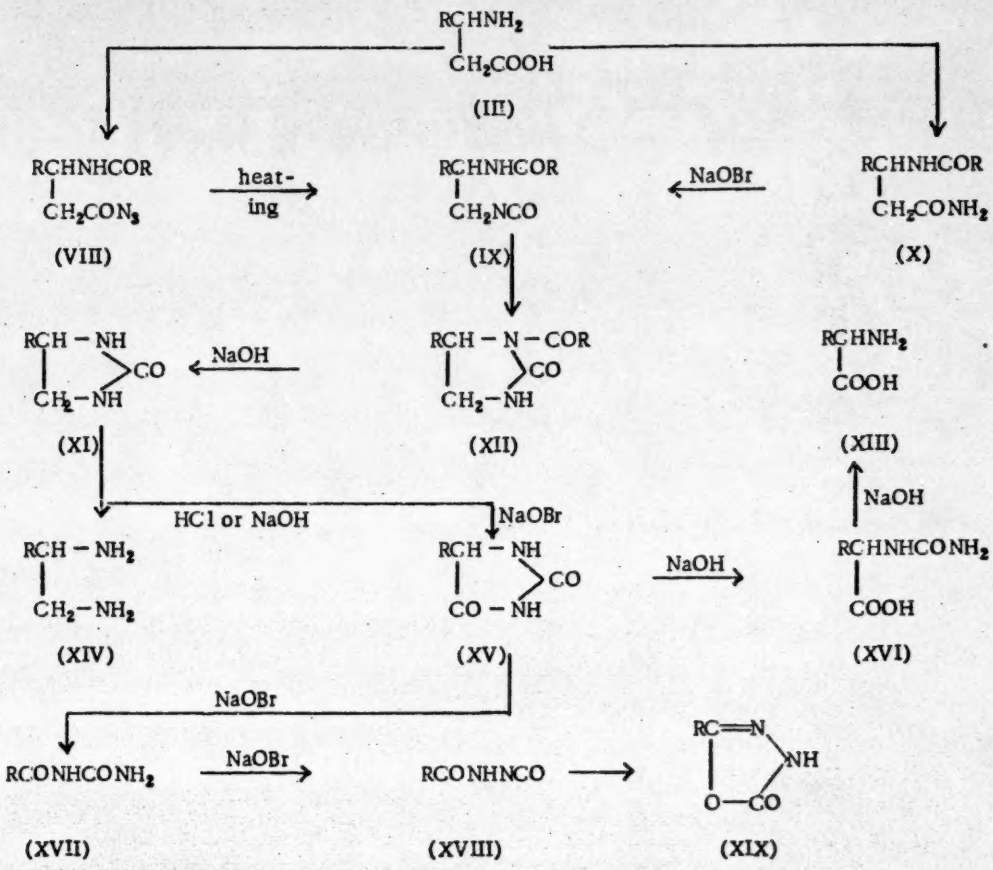
Scheme 1



Of no less value are methods for synthesis of substituted glyoxylidones of the type (XI) and (XII) which were discovered and developed in detail by V. M., and which previously had been found to be relatively or completely unavailable substances. A variety of representatives of these two types of heterocyclic compounds can at present be readily obtained from β-amino acids by the following procedures: (III) ⟶ (VIII) ⟶ (IX) ⟶ (XII) ⟶ (XI) or (III) ⟶ (X) ⟶ (IX) ⟶ (XII) ⟶ (XI) (see Scheme 2). A thorough study of the latter reaction carried out quite recently by V. M. has led to very interesting results. He has demonstrated the feasibility of converting β-amino acids not only into glyoxylidones (XI) and (XII), but also into other types of heterocyclic compounds – hydantoins (XV) and hydroxydiazolones (XIX); moreover, there

was found the possibility for a very original and at the same time simple conversion of β-amino acids (III) to α-amino acids (XIII). The mechanism for all of these complex conversions presented in Scheme 2 has been experimentally confirmed, and at the present time is found to be proved correct. These exceptionally fine works of V. M. characterize splendidly the profoundness and intricacy of his experimental and theoretical research.

Scheme 2



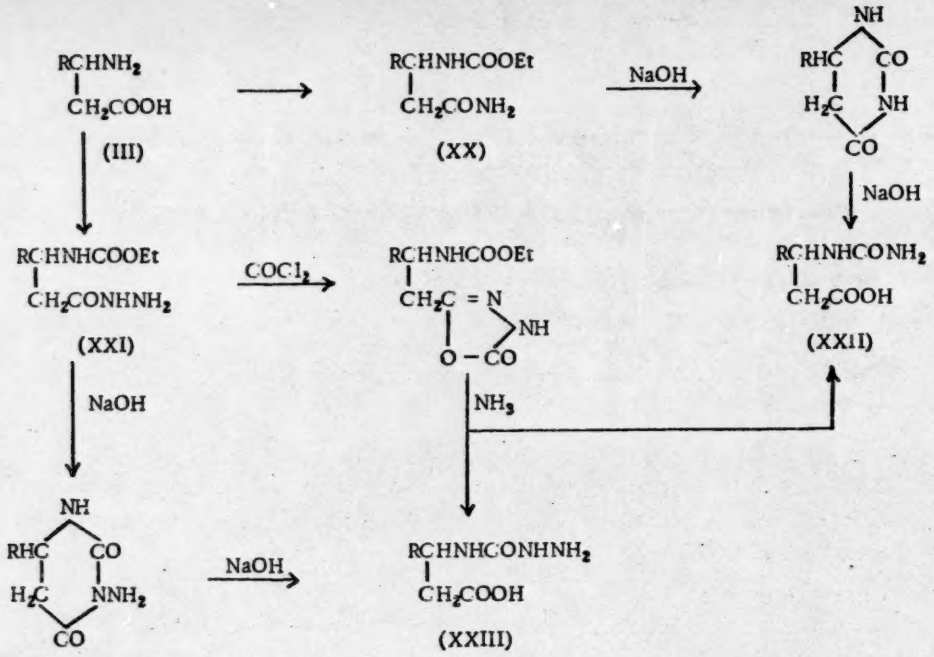
A thorough study of various conversions of β-amino acids has recently led V. M. to the discovery of specific means of transition from derivatives of β-amino acids of the types (XX) and (XXI) to β-ureido-(XXII) and to β-semicarbazido acids (XXIII) (see Scheme 3). In 1952-1953 V. M. demonstrated that the conversion of hydrazides of N-carboethoxylated β-amino acids (XXI) into β-semicarbazido acids (XXIII) under the influence of caustic alkali is a general and very simple method for synthesizing these previously unknown compounds.

This remarkable cycle of investigations by V. M., achieved mainly by him in the most recent years, has established the feasibility of obtaining with great ease from β-amino acids, not only their various derivatives and analogs, but also many types of heterocyclic compounds as well, and also conversion of β-amino acids to the corresponding α-amino acids. The significance of these investigations is sufficiently evident from both a theoretical and a practical viewpoint.

Along with the investigations cited, V. M. Rodionov has recently published, jointly with B. M. Bogoslovsky, M. A. Gubareva, Z. S. Kazakova, N. N. Suvorov, A. M. Fedorova, M. G. Chentsova and L. V. Shagalov a series of interesting works [23-32] pertaining to a study of synthetic procedures, as well as the properties of various heterocyclic compounds which are derivatives of pyrazolone, imidazole, indole, thionaphthene, tetrahydroisoquinoline and benzophenanthridine. Synthesis of this latter type was undertaken in connection with a study of synthetic methods for chelidonine – an alkaloid contained in celandine (Chelidonium majus).

For the past five years, V. M. Rodionov, with a number of coworkers (V. N. Belov, R. Sh. Grigoryeva, T. S. Kiseleva, S. A. Kore, I. V. Machinskaya, G. I. Moldivanskaya, E. A. Ogorodnikova, E. F. Polunina, K. S. Polyakova,

Scheme 3



E. L. Simanovskaya, E. K. Smolyaninova, N. N. Shevyakova and others), has paid considerable attention to a study of synthetic procedures and the properties of many carbonyl-containing compounds: aldehydes, ketones, γ-diketones, β- and γ-keto acids and their esters [26, 27, 31, 33-49].

About 30 different aldehydes and ketones of aliphatic, alicyclic, aromatic and heterocyclic series have been either synthesized for the first time, or their methods of preparation have been substantially modified and considerably improved. These works were undertaken in order to obtain various carbonyl-containing aromatic substances and to study the problem of relationship between their structures and aroma, as well as to have readily accessible raw materials (aldehydes) for synthesis of β-amino acids. Of the total research work carried out, a considerable number of various aldehydes and ketones were obtained in good yields, and several general synthetic procedures were worked out for carbonyl-containing aromatic substances. Thus, for example, V. M. Rodionov, V. N. Belov, and others, proposed a very successful procedure for synthesizing monosubstituted acetoacetic acid esters directly from the sodium salt of acetoacetic ester, which is formed by condensation of ethyl acetate; this method is of great technological value for perfume manufacture since it is possible in principle to develop simple synthetic means for producing a series of substituted aldehydes (via the corresponding ketones and esters of glycidic acids).

Among other investigations of V. M. which are devoted to works on carbonyl-containing compounds, there should be mentioned works in which are described a new method for synthesis of γ-diketones (from α-haloketones and sodium acetoacetate), a simple method for converting acetoacetic ester into nitroacetic ester (through isonitrosoacetoacetic ester, and its subsequent oxidation by H_2CrO_4), the properties of γ-chloro- and α,γ-diphenylacetoacetic esters, synthesis and properties of δ-chlorolevulinic acid, and the transformations of cotarnine, hydrastinine and their benzoyl derivatives under the effect of alkali. The majority of these works were for the purpose of finding methods for synthesizing various types of heterocyclic compounds as mentioned briefly above.

Investigation on the chemistry of aromatic compounds, which has recently been intensively developed by V. M. Rodionov with a number of his coworkers, is not limited to a study of carbonyl-containing compounds only. Syntheses of other types of substances – aromatic and alicyclic hydrocarbons, phenols, alcohols, esters and others – have also been achieved. In this connection, isopropylation and isobutylation processes for benzene and phenols, reactions of partial and exhaustive hydrogenation of benzanthrone, and certain other conversions have been thoroughly studied [39, 41-43, 45, 47, 49, 50].

The research field covered by V. M. Rodionov has widened and expanded our knowledge of the chemistry of carbonyl-containing, and other types of organic compounds, but to a particular degree has favored the creation of a series of standard procedures for synthesizing aromatic substances, making it possible to realize the synthesis of many compounds valuable in perfume manufacture, and has provided an opportunity for discovering certain relationships between the structure of organic molecules and their odors.

Apart from the large number of experimental papers which V. M. Rodionov has published over the past several years, he has, in that time, also written numerous reviews [51-55] (on the chemistry of alkaloids, β-amino acids, and dyes, relative to development of Soviet organic chemical industry), articles on technological-economic problems [57-58], reviews (for example, in connection with publications of selected works by A. M. Butlerov [56]), and biographical essays concerning the works and life activities of prominant Russian and Soviet scientists – D. I. Mendeleev, A. M. Butlerov, N. D. Zelinsky, N. M. Kizhner, A. P. Orekhov, N. N. Vorozhtsov, A. E. Porai-Koshits, A. M. Berkengeim, S. I. Kanevskaya [59-64].

Such intensive and productive work as V. M. Rodionov continuously puts out right up to the present must be admired.

The years pass, but Vladimir Mikhailovich changes but little. Although his hair has become white, his eyes as before are youthful, and as before, they light up and sparkle during an absorbing discussion, and as before, the eyes are lit by a keen, questioning mind, or there is reflected in the eyes a profound, creative, intrinsic activity. Vladimir Mikhailovich is so consumed with eagerness to work and to create, so full of lively and stimulating energy, that there remains only to wish him the preservation of these remarkable characteristics for many years to come.

Listing of the Works of V. M. Rodionov, Published in the Interim 1948-1953.*

1. Investigation in the Field of Tetrahydropyrimidinic Compounds. Synthesis of 4-Phenyl-6-hydroxytetrahydropyrimidine Derivatives. J. Gen. Chem., 18, 1912 (1948) (With the Participitation of V. V. Kiseleva).

2. Interaction of β-Phenyl-β-alanine with Hypobromite. Synthesis of 4-Phenyl Glyoxylidone and Its Acyl Derivatives. J. Gen. Chem., 18, 1905 (1948) (With the Participitation of V. V. Kiseleva).

3. Investigation in the Field of β-Amino Acids. Synthesis of β-Guanidino Acids and Their Conversion to Hexahydropyrimidines. J. Gen. Chem., 18, 2023 (1948) (O. S. Urbanskaya Participating).

4. Conversion of β-Alkyl-(Aryl)-β-N-carbethoxyaminopropionic Acid Amides into β-Ureido Acid. Proc. Acad. Sci. 65, 853 (1949) (V. K. Zvorykina Participating).

5. Interaction between Amino Acid Hydrochlorides and Ethylene Oxide. Bull. Acad. Sci., USSR, Div. Chem. Sci. 108 (1950), (N. G. Yartseva Participating).

6. Structure of 1-Naphthaldehyde-8-carboxylic Acid. Bull. Acad. Sci. USSR, Div. Chem. Sci., 247 (1950) (A. M. Fedorova Participating).

7. Condensation Reaction of Py-Indolealdehydes with Malonic Acid and with Cyanoacetic Ester. J. Gen. Chem., 20, 2202 (1950) (T. K. Veselovskaya Participating). [See page 2287]**

8. New Data on the Hofmann Reaction. Article III. Interaction of Acylated Amides of β-Aminopelargonic Acid with Alkaline Hypobromites. Bull. Acad. Sci. USSR, Div. Chem. Sci., 608 (1950) (V. K. Zvorykina Participating).

9. New Data on the Hofmann Reaction. Article IV. Interaction of N-Acylated β-Phenyl-β-alanine Amides. Bull. Acad. Sci. USSR, Div. Chem. Sci., 57 (1951) (V. V. Kiseleva Participating).

10. Synthesis and Characterization of β-(β-Naphthyl)-β-aminopropionic Acid and Some of Its Derivatives. Bull. Acad. Sci. USSR, Div. Chem. Sci., 113 (1952) (B. I. Kurtev Participating). [See page 123.]

11. β-(β-Naphthyl)-β-aminopropionic Acid and Its Pyrimidine Derivatives. Bull. Acad. Sci. USSR, Div. Chem. Sci., 268 (1952) (B. I. Kurtev Participating). [See page 285].

12. Synthesis and Characterization of β-(α-Naphthyl)-β-aminopropionic Acid. Proc. Acad. Sci., 82, 269 (1952) (N. A. Kravchenko Participating).

13. Synthesis of β-(Cyclohexyl)-β-aminopropionic Acid and Some of Its Derivatives. Bull. Acad. Sci. USSR, Div. Chem. Sci., 278 (1952) (T. S. Kiseleva Participating). [See page 293].

14. A New Synthesis of Alkyl Esters of β-Amino Acids. Bull. Acad. Sci. USSR, Div. Chem. Sci., 696 (1952) (N. N. Bezinger Participating). [See page 637.]

15. The Curtius Reaction with a Series of β-Amino Acids. Bull. Acad. Sci. USSR, Div. Chem. Sci., 962 (1952) (N. N. Bezinger Participating). [See page 847.]

*A list of the earlier works of V. M. Rodionov can be found in J. Gen. Chem., 18, 1894 (1948) and in Chem. Prog. 17, 543 (1948).

** Here, and subsequently in this listing, numbers in brackets indicate the pagination of the Consultants Bureau English Translation of the paper listed.

16. A General Procedure for Synthesis of β-Semicarbazido Acids. Proc. Acad. Sci., 85, 579 (1952) (V. K. Zvorykina Participating).

17. Investigation in the Field of β-Amino Acids. Synthesis and Conversions of β-Aminobutyric Acid. Bull. Acad. Sci. USSR., Div. Chem. Sci., 103 (1952) (N. G. Yartseva Participating). [See page 113].

18. Synthesis of 5-Alkylated 1,3,4-Hydroxydiazolones and A Study of Their Interaction with Ammonia. Bull. Acad. Sci. USSR, Div. Chem. Sci., 70 (1953) (V. K. Zvorykina Participating). [See page 61].

19. New Data on the Hofmann Reaction. Comm.V. Interaction of N-Acylated-β-aryl-β-alanines Amides with Alkaline Hypobromite. Bull. Acad. Sci. USSR, Div. Chem. Sci., 513 (1953) (V. V. Kiseleva Participating). [See page 461].

20. On the Characteristics of Phthalimidineacetic Acid. J. Gen. Chem., 23, 396 (1953) (E. I. Chukhina Participating). [See page 403.]

21. Research in the Field of β-Amino Acids. Synthesis of β-(β-Decalyl)-β-amino Propionic Acid and its Characterization. Bull. Acad. Sci. USSR, Div. Chem. Sci., 253 (1953) (L. V. Antik Participating). [See page 231].

22. Synthesis of β-(N-Methyl)-amino-β-phenylpropionic Acid and Its Derivatives. J. Gen. Chem., 23, 983 (1953) (E. V. Yavorskaya Participating). [See page 1025.]

23. Synthesis and Investigation of Azo Dyes. Derivatives of 3-Hydroxythionaphthene. J. Appl. Chem., 21, 962 (1948) (B. M. Bogoslovsky and Z. S. Kazakova Participating).

24. Synthetic Investigation in the Field of Chelidonium majus Alkaloids., Proc. Acad. Sci., 69, 189 (1949) (N. N. Suvorov Participating).

25. Synthetic Investigations in the Field of Alkaloids. Proc. Acad. Sci., 75, 43 (1950) (N. N. Suvorov Participating).

26. Hydrazones of α,γ-Diphenylacetoacetic Ester. J. Gen. Chem., 20, 1273 (1950) (N. N. Suvorov Participating). [See page 1323]

27. Interaction of Cotarnine and Hydrastinine and Their Benzoyl Derivatives with Alkali Hydroxides. J. Gen. Chem., 21, 321 (1951) (M. G. Chentsova Participating). [See page 353].

28. A New Method for Formation of Thioindigo on Fiber. J. Appl. Chem., 22, 670 (1951) (B. M. Bogoslovsky and Z. S. Kazakova Participating). [See page 757].

29. New Data in the Field of Chemistry of Pyrazolone Derivatives. Bull. Acad. Sci. USSR, Div. Chem. Sci., 1049 (1952) (A. M. Fedorova Participating). [See page 917].

30. Synthesis of 6-Carboxy-11-methyl-5,6,13,14-tetrahydro-1,2-benzophenanthridine. Proc. Acad. Sci., 82, 731 (1952) (N.N. Suvorov and L. V. Shagalov Participating).

31. New Data on Condensation of γ-Chloroacetoacetic Ester and a Synthesis of δ-Chlorolevulinic Acids. J. Gen. Chem., 23, 1830 (1953) (M. A. Gubareva Participating). [See page 1933.]

32. Synthesis of 2-Mercaptoimidazolylpropionic Acid. J. Gen. Chem., 23, 1845 (1953) (M. A. Gubareva Participating). [See page 1951.]

33. Synthesis of α-Nitrosubstituted Carboxylic Acid Esters. Article I. Nitroacetoethyl Ester. J. Gen. Chem., 18, 917 (1948) (I. V. Machinskaya and V. M. Belikov Participating).

34. New Synthesis of γ-Diketones, Proc. Acad. Sci., 68, 535 (1949) (E. F. Polunina Participating).

35. Synthesis of Phthalide from Phthalic Anhydride. J. Appl. Chem., 22, 853 (1949) (E. I. Chukhina Participating).

36. Synthesis of Monosubstituted Acetoacetic Esters Without the Use of Free Acetoacetic Ester. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances, No. 1, p. 5 (1952) (V. N. Belov, E. A. Ogorodnikova and N. N. Shevyakova Participating).

37. Synthesis of Aromatic Substances on the Basis of Monosubstituted Acetoacetic Esters. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. 1, page 6 (1952) (V. N. Belov, E. A. Ogorodnikova and N. N. Shevyakova Participating).

38. Effect of α,β-Unsaturated Aldehyde and Ketone Double Bonds Upon the Condensing Power with Chloroacetic Acid Ester. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. 1, p. 7 (1952) (E. A Ogorodnikova and G. I. Moldovanskaya Participating).

39. Effect of Structural Isomerism Upon Odor in A Series of Triisopropylbenzyl Alcohols and Triisopropylbenzaldehydes. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. I, p. 27 (1952) (V. N. Belov and S. A. Kore Participating).

40. Synthesis of 3-(β-Naphthyl)-2-methylpropanal. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. I, p. 33 (1952) (V. N. Belov and R. Sh. Grigoryeva Participating).

41. Synthesis of p-Tertiarybutylcyclohexylacetate and p-Tertiarybutylcyclohexanone. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. I, p. 38 (1952) (V. N. Belov and E. A. Simanovskaya Participating).

42. Synthesis of Tertiary-butyl-β-decallylacetate and Tertiary-butyl-β-decalone. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances, No. I, p. 39 (1952)(V. N. Belov and E. A. Simanovskaya Participating).

43. Transformation Reaction of 4-Hydroxy-3-ethoxyphenylglycolic Acid and Vanillal. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances, No. I, p. 43 (1952). (K. S. Polyakova Participating).

44. Synthesis of Dihydrocivetone. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. I, p. 46 (1952) (E. K. Smolyaninova Participating).

45. Hydrogenation of Benzanthrone. Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances. No. I, p. 47 (1952) (V. N. Belov, E. K. Smolyaninova, A. A. Baga and A. A. Bugorkova Participating).

46. Synthesis of the Diethyl Ester of Hexadecandicarboxylic Acid. Ibid. p. 63 (1952) (E.K.Smolyaninova Participating).

47. Transformation of Glyoxylic Acid in Alkaline Medium. Ibid. p. 66(1952)(K.I. Bogacheva Participating).

48. New Synthetic Method for Deriving Aulepine Derivatives. Ibid. p. 68(1952)(K.S. Polyakova Participating).

49. Synthesis of Phenylacetic Acid. Ibid. p. 71 (1952) (E. K. Smolyaninova Participating).

50. Isolation of Pure p-Cresol and Synthesis of p-Cresol Esters. Ibid. No. I, p.64(1952)(V. P. Osipova and L. B. Gurevich Participating).

51. New Data on β-Amino Acid Chemistry. Prog. Chem., 20, 273 (1951).

52. Reaction Mechanism Between Amides of N-Acylated β-Amino Acids and Alkaline Solutions of Hypobromite. Works of the Council on Problems of Organic Reaction Mechanisms, Kiev (1952).

53. Kizhner Reaction. Symposium on Reactions and Investigational Methods for Organic Compounds, Book I, p. 7, State. Chem. Press, Moscow (1951) (N. G. Yartseva Participating).

54. The Chemistry of Alkaloids, Its Significance, and Future Problems. Bull.Acad.Sci.USSR. Div. Chem. Sci., 385 (1953). [See page 351.]

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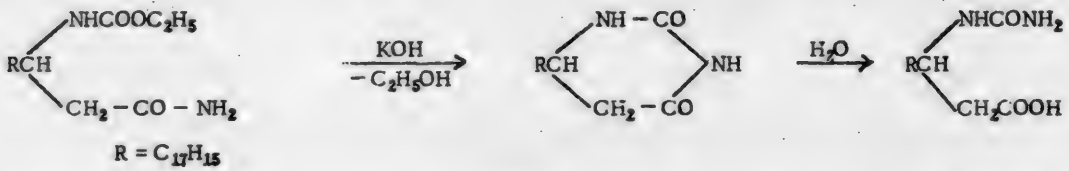
β-AMINOCAPRIC ACID AND ITS CONVERSIONS

V. M. Rodionov, V. K. Zvorykina and N. E. Kozhevnikova

β-Aminocapric acid and 4-heptyl-2,6-dihydroxyhexahydropyrimidine have been synthesized by K. Lang and F. Addickes [1]. The authors succeeded in determining the presence of dihydrouracil in the urine of experimental animals while feeding a diet containing β-amino acids.

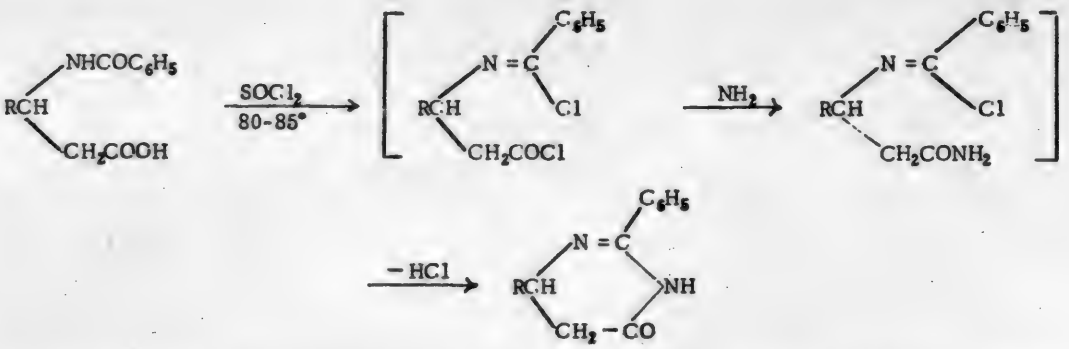
Having extended β-amino acid syntheses according to Rodionov from new aldehydes of the aliphatic series, the present authors have undertaken the problem of obtaining new homologs of β-amino acids and of confirming common reactions found for β-amino acids by the authors.

The following derivatives of β-aminocapric acid were synthesized: β-carboethoxy- derivative, its amide, the N-benzoyl derivative and its amide and the β-ureido acid. The latter was obtained by both the usual method by reacting β-aminocapric acid with potassium cyanate, and also by heating with 5% KOH, a solution of β-(N-carboethoxy)-aminocapric acid amide, i.e., according to a reaction established for the first time by the authors, using β-(N-carboethoxy)aminopelargonic acid amide as an example, and verified on a series of other β-amino acids [2].



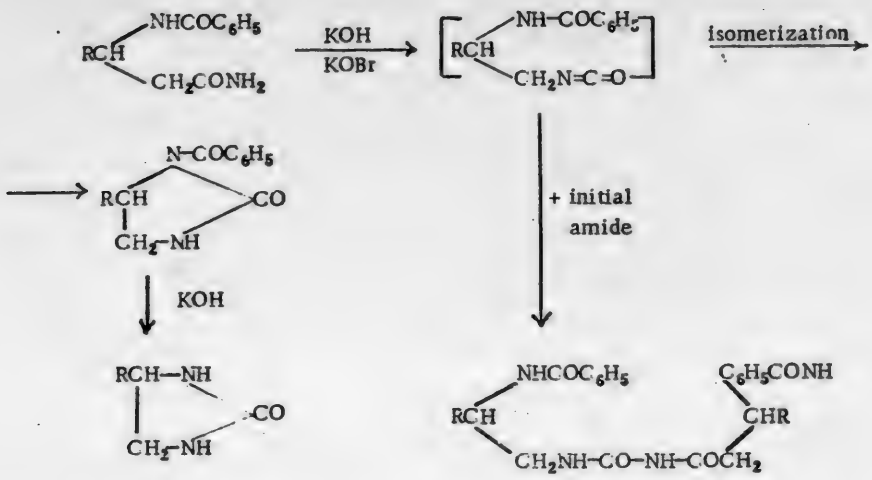
R = $C_{17}H_{15}$

2-Phenyl-4-heptyl-6-hydroxytetrahydropyrimidine was synthesized according to the thionyl chloride method which is standard for benzoyl derivatives of β-amino acids [3] which have been synthesized so far:



By reacting an alkaline hypobromite solution with the benzoyl amide derivative of β-aminocapric acid, it was possible to isolate four substances: 5-heptylglyoxalidone, 1-N-benzoyl-5-heptylglyoxalidone, benzoic acid, and a substance with m.p. 216°, which, according to elementary analysis data, was found to be a urea derivative. On the basis of products isolated, it was possible to deduce that the reaction proceeds in the following manner (see top of following page).

Formation of 1-N-benzoyl-5-heptylglyoxalidone (product of the intramolecular isomerization of the isocyanic ester) during this reaction again confirmed the correctness of the scheme proposed by the authors [4].



To verify the structure of 1-N-benzoyl-5-heptylglyoxalidone, its hydrolysis was carried out with 20% KOH solution. 5-Heptylglyoxalidone and benzoic acid were isolated.

As side-products in the synthesis of β-aminocapric acid, an unsaturated acid with an equivalent weight of 264 (evidently a mixture of decylenic acid and heptylbutyrolactone), and caprylic acid, were separated. Formation of caprylic acid should be related to a partial disproportionation of the initial aldehyde. Feasibility of a similar reaction was earlier observed during the synthesis of β-aminopelargonic acid, wherein it was possible to isolate both products of the aldehyde disproportionation: enanthic acid in the form of its compound with a molecule of β-aminopelargonic acid (a substance with m.p. 140°, crystallizing from water and stable after dissolution in alkali and separation from the acid), and heptyl alcohol.

EXPERIMENTAL.

Synthesis of β-Aminocapric Acid

22 ml of 8.1% alcoholic NH_3 solution was added with cooling (ice and salt) to 12 g of octanal, the mixture cooled for 30 minutes, and 9.75 g of finely powdered malonic acid then introduced with stirring. The flask was connected with descending condenser and then heated for 1.5 hours at 70°, followed by 7 hours on a boiling water bath. A transparent yellow oil resulted, from which, upon cooling, crystals separated. The condensation product was treated several times with hot water and siphoned. The aqueous layer was decanted off from traces of oil and concentrated to small volume. There resulted 2.25 g of β-aminocapric acid, with m.p. 202° (18.7%, calculating on the basis of malonic acid used for reaction). Fine, colorless crystals resulted after recrystallization from water, with m.p. 205-206°.

β-Aminocapric acid is readily soluble in alcohol, dilute mineral acids and alkalies, as well as in hot water – poorly so in cold water, soda, ammonia, and insoluble in ether and benzene.

With further evaporation of the filtrate, 3 g of malonic acid plus ammonium malonate resulted.

Found %: C 63.81, 63.90; H 11.46, 11.31; N 8.17, 8.14. $C_{10}H_{21}O_2N$. Calculated %: C 64.17; H 11.20; N 7.48.

The oil separated from the aqueous layer – about 3.7 g – which gave reaction for double bond. By washing the oil obtained from several experiments with soda solution, the acid was isolated as a light-yellow oil.

0.127, 0.1083 g substance: Used for titration: 7.5, 6.3 ml KOH (T = 0.004882). Equivalent weight found: 138.7, 140.8. $C_8H_{16}O_2$. Equivalent weight calculated: 144.

Synthesis of the Amide. 0.71 g of the acid and 0.49 g of thionyl chloride were heated at 40° for 3 hours. The reaction product was soluble in ether and in saturated NH_3. After distilling off the ether, there resulted a partially crystallized oil. The crystals were filtered off and recrystallized from water. Scaly platelets with m.p. 94-96° (m.p. 105-106° according to the literature data).

Found %: N 9.91. $C_8H_{17}ON$. Calculated %: N 9.78.

After washing with soda, the oil was dissolved in ether and treated with 10% NaOH. Traces of oil were separated from the alkaline solution. After alkali, the ether solution was washed several times with water. Part of the oil from the ether layer went into the wash waters. Upon acidification, oil separated, which was extracted with ether; the ether solution was washed three times with water, dried with Na_2SO_4, and distilled. A yellow, transparent oil resulted, giving a reaction for double bond.

0.0873, 0.1254 g substance: Used for titration: 2.7, 3.9 ml KOH. Equivalent weight found: 264.8, 263.8. $C_{10}H_{18}O_2$. Equivalent weight calculated: 170.

A large equivalent weight indicated presence of lactone in the acid isolated.

Synthesis of β-Ureidocapric Acid

1 g of β-aminocapric acid was dissolved, with heat, in 40 ml of water. 0.5 g of potassium cyanate was added, with cooling, and heating then carried out for 4 hours on a rapidly boiling water bath. The slightly turbid solution was filtered off and acidified to Congo red with HCl and with efficient cooling. The resulting white crystalline precipitate was filtered off, washed with water and dried. 0.8 g (65%) of crystals resulted, with m.p. 125-127°. After recrystallization from hot water, there resulted colorless needles: 0.12 g with m.p. 129-130°, and 0.61 g from the mother liquor, with m.p. 122-127°.

Found %: C 57.2, 57.18; H 9.74, 9.63; N 12.10, 12.00. $C_{11}H_{22}O_3N_2$. Calculated %: C 57.39; H 9.56; N 12.17.

Synthesis of 4-Heptyl-2,6-dihydroxyhexahydropyrimidine

0.6 g of β-ureidocapric acid was heated for 1 hour on a wire gauze with 10 ml of HCl (1:1). Upon cooling a white precipitate separated from the solution in the form of long, thin needles. The precipitate was filtered off, washed with a small amount of water, and recrystallized from dilute alcohol (4:1). There resulted 0.4 g of long, colorless needles with m.p. 181-182° (yield 72.3% of theory).

Found %: N 13.38, 13.51. $C_{11}H_{20}O_2N_2$. Calculated %: N 13.21.

Synthesis of β-(N-Carbethoxyamino)-capric Acid

0.5 g of an ethyl ether solution of chlorocarbonic acid was added dropwise, with cooling, to 1 g of β-aminocapric acid in 10% sodium hydroxide solution (0.67 g) at 0°. The solution was allowed to stand for 1 hour at room temperature, and then, with cooling, was acidified with HCl to Congo red. A white, crystalline precipitate resulted in the amount of 0.79 g (52.1%), m.p. 69-70°.

Found %: C 59.92, 60.01; H 9.53, 9.43; N 5.99, 5.80. $C_{13}H_{25}O_4N$. Calculated %: C 60.23; H 9.65; N 5.41.

Synthesis of the Amide. 0.62 g of the carboethoxy derivative was heated to 40° with 0.28 g (theoretical amount) of thionyl chloride to the cessation of gas bubble evolution. The resulting orange oil was dissolved in 100 ml of dry ether, cooled to −10°, saturated with NH_3, and left to stand overnight. The amide was filtered off, washed with 5% KOH, then with water, and dried. Weight of resulting amide was 0.26 g (43%). After distilling off the ether solution, 0.2 g of non-crystallizing oil resulted. After recrystallization from methyl alcohol with several drops of water added, the resulting amide melted at 152-152.5°. Fine colorless needles.

Found %: C 60.24, 60.31; H 10.20, 10.28; N 10.64, 10.78. $C_{13}H_{26}O_3N_2$. Calculated %: C 60.46; H 10.07; N 10.85.

Synthesis of β-Ureidocapric Acid and 4-Heptyldihydrouracil from β-(N-Carbethoxyamino)capric Acid Amide

0.4 g of the amide was heated on a wire gauze for 1.5 hours with 20 ml of 5% NaOH. The product was cooled to −5° and acidified to Congo red with HCl. There resulted a white, crystalline precipitate of the ureido acid. 0.16 g with m.p. 126-128° was obtained. A sample mixed with the ureido acid isolated previously (m.p. 129-130°) melted at 126-128°.

Found %: C 57.22, 57.27; H 9.61, 9.70; N 11.65, 11.50. $C_{11}H_{22}O_3N_2$. Calculated %: C 57.39; H 9.56; N 12.17.

Synthesis of 4-Heptyldihydrouracil

0.15 g of ureido acid was converted into dihydrouracil under the conditions described above. Crystals with

m.p. 181-182° resulted. A sample mixed with dihydrouracil isolated earlier also melted at 181-182°.

Found %: N 13.26. $C_{11}H_{20}O_2N_2$. Calculated %: N 13.21.

Synthesis of β-(N-Benzoylamino)-capric Acid

0.9 g of benzoyl chloride was added dropwise to a solution of 1 g of β-aminocapric acid in 10 ml of 12 N KOH, with cooling to 0°. Following addition of the total amount, stirring was carried on for 1 hour, and then the solution extracted with ether to remove benzoyl chloride excess, cooled, and acidified with HCl to Congo red. A white voluminous precipitate resulted. To remove benzoic acid, it was boiled three times with 50 ml of water, filtered, and dried at 100°. 1.1 g (75.4%), with m.p. 133-134°, resulted. The benzoyl derivative is practically insoluble in hot water; it can be recrystallized from 50% alcohol. It precipitates in the form of very fine needles.

Found %: C 70.04, 69.88; H 8.54, 8.69; N 4.95, 5.01. $C_{17}H_{25}O_3N$. Calculated %: C 70.10; H 8.59; N 4.81.

Synthesis of the Amide. 7.6 g of the benzoyl derivative was heated to 40° with 3.08 g of thionyl chloride to cessation of bubble evolution (about 3 hours). 800 ml of dry ether was put in the flask, the solution cooled to −10°, and saturated with NH_3. The precipitate was filtered off after 12 hours, dried and washed with 5% KOH and water, and then dried again. 7.1 g of amide resulted (93.5%). Upon recrystallization from 70 ml of ethyl alcohol, there resulted 5 g with m.p. 183-184°, and from the mother liquor, 1.9 g with m.p. 163-175°. Colorless needles.

Found %: C 70.08, 70.00; H 9.13, 9.05; N 9.99, 9.89. $C_{17}H_{26}O_2N_2$. Calculated %: C 70.34; H 8.96; N 9.66.

Synthesis of 2-Phenyl-4-heptyl-6-hydroxytetrahydropyrimidine

1.7 g of benzoyl derivative was heated with 2.07 g of thionyl chloride to 80-85°, until bubble evolution ceased. The thionyl chloride excess was distilled off in vacuo and the residue dissolved in 200 ml of absolute ether and saturated with NH_3. No precipitate was obtained. After 12 hours, the ether solution was distilled to one-third of the initial volume and cooled. The resulting precipitate was filtered off and recrystallized from dilute alcohol. The resulting substance melted at 170°. A sample mixed with amide (m.p. 183-184°) melted at 178-180°. Upon further distillation of ether, a non-crystallizing oil resulted. Upon treatment (with heat) with petroleum ether, a portion went into the ether solution. Upon cooling there precipitated from the ether a white crystalline precipitate (long thin needles), m.p. 87-89°. Upon recrystallization from dilute alcohol, the melting point did not change.

Found %: N 10.10, 9.94. $C_{17}H_{24}ON_2$. Calculated %: N 10.29.

A Hofmann Reaction with the Amide of the Benzoyl Derivative of β-Aminocapric Acid

5 g of amide pre-cooled to −10° was added in small portions, with stirring, over a period of 5 hours, to a solution of potassium hypobromite (obtained from 2.5 ml of Br_2 and 9.5 g of KOH in 45 ml of water). After dissolution of the amide, the yellow transparent solution was stirred for another hour and the flask then heated on a water bath to 55°. Heating was terminated and the temperature rose spontaneously to 60°. At this time, there was observed discoloration and turbidity of the solution, and the formation of a precipitate. The reaction mass was again heated to 65°, and then immersed in a cooling mixture. The resulting slightly colored oil (II) was separated and the alkaline solution (I) extracted three times with ether. The oil (II) was treated with the same ether. Upon dissolution in ether, there resulted 0.65 g of voluminous precipitate (III). The ether solution was washed several times with HCl (1:2) (IV).

Isolation of 4-Heptylglyoxalidone Hydrochloride (IV). The acid solution (IV) was extracted with ether and with efficient cooling (ice-salt) was made alkaline with solid KOH. A small amount of crystals resulted. They were extracted with ether and the ether distilled off. 0.22 g of white crystalline material resulted. After recrystallization from a mixture of ethyl ether and petroleum ether, m.p. was 111-112°. A sample mixed with 1-benzoyl-4-heptylglyoxalidone (m.p. 105-106°) melted at 78-82°.

Found %: C 65.03, 65.13; H 11.01, 10.85; N 15.29, 15.39. $C_{10}H_{20}ON_2$. Calculated %: C 65.21; H 10.86; N 15.21.

Isolation of 1-N-Benzoyl-5-heptylglyoxalidone. The ether solution (II) after washing with hydrochloric acid was then washed with 5% KOH solution, followed by water and then distilled. There resulted after recrystallization from petroleum ether, 2.22 g of 1-N-benzoyl-5-heptylglyoxalidone, m.p. 105-106°. Colorless thin needles. A sample mixed with heptylglyoxalidone (m.p. 111-112°) melted at 79-82°.

Found %: C 70.41, 70.30; H 8.45, 8.57; N 9.65, 9.57. $C_{17}H_{24}O_2N_2$. Calculated %: C 70.83; H 8.33; N 9.72.

Investigation of the Alkaline Solution (I). A small precipitate resulted from the alkaline solution of hypobromite (I) upon acidification with HCl (to which had been added beforehand several drops of sodium bisulfite); it was extracted with ether and the ether distilled off. There resulted 0.34 g of acid with m.p. 118-120° A sample mixed with benzoic acid melted at 120-122°.

Investigation of the Precipitate (III). The precipitate resulting from dissolution of oil in ether was washed several times by boiling with alkali and water. Upon acidification of the alkaline wash water, there resulted an acid with m.p. 114-116°, insoluble in hot water, poorly so in ether, readily in alkali and alcohol. With repeated dissolution in alkali and precipitation with acid, the m.p. increased to 128-129° A sample mixed with the benzoyl derivative of β-aminocapric acid (m.p. 133-134°) melted at 130-131°.

The residue washed out from the benzoyl derivative was washed with HCl and water, and then recrystallized 3 times from alcohol. Fine, thin colorless needles resulted with m.p. 216°.

Found %: C 69.62, 69.75; H 8.65, 8.78; N 9.78, 9.95. $C_{34}H_{50}O_4N_4$. Calculated %: C 70.59; H 8.65; N 9.68.

Saponification of 1-N-Benzoyl-5-heptylglyoxalidone. 0.5 g of benzoylglyoxalidone (m.p. 105-106°) was heated with stirring on a boiling water bath with 7 ml of 20% KOH for 5 hours. The flask contents were extracted with ether and the ether solution treated several times with HCl (1:2). The cooled (ice and salt) acid solution was alkalized with solid KOH and the heptylglyoxalidone extracted with ether. After distillation of the ether, there resulted 0.05 g of colorless needles, m.p. 110-112°. A sample mixed with heptylglyoxalidone, separated earlier (m.p. 111-112°), melted at the same temperature and with benzoylglyoxalidone, at 78-95°. The alkaline mother liquor was acidified with HCl and extracted with ether. After distillation of the ether, there resulted an acid with m.p. 118-121°. A sample mixed with benzoic acid melted at 121-122°.

SUMMARY

1. Synthesis of β-aminocapric acid by interaction of N-octanal with malonic acid in the presence of ammonia has been carried out; the resulting β-amino acid has been characterized by preparation of the following acyl derivatives: urethane, N-benzoyl, and the amides.

2. Synthesis of β-ureidocapric acid has been carried out in two ways: 1) by reacting the β-amino acid with potassium cyanate, and 2) by treating the amide of N-carbethoxy-β-aminocapric acid with dilute alkali. The ureido acid has been converted to the 4-heptyldihydrouracyl derivative in the usual manner.

3. Using a standard method developed in the authors' laboratory, 2-phenyl-4-heptyl-6-dihydroxytetrahydropyrimidine has been prepared from N-benzoyl-β-aminocapric acid.

4. As an example of the Hofmann reaction, carried out with N-benzoyl-β-aminocapric acid amide, reaffirmation has been made of a scheme for intramolecular isomerization of the isocyanic ester, resulting in the formation of the corresponding 1-N-benzoyl-5-heptylglyoxalidone.

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SOLUBILITIES OF SOME β-AMINO ACIDS

V. V. Monblanova and V. M. Rodinov

Interest in β-amino acids has increased markedly over the past decade. It has been found that certain β-amino acids enter into the composition of vitamins and antibiotics, but, at the same time, there do not exist in the literature, papers on research into the physico-chemical properties of these compounds. β-Alanine has attracted most attention on the part of investigators; its solubility in water and in water-alcoholic solutions [1] has been determined, as well as its acid and alkaline dissocation constants [2,3].

A task of the present work has been a quantitative study of the solubility of the β-amino acids in water in relation to their molecular structures, and the effect of hydrogen ion concentration upon the solubility of poorly-soluble acids. β-Phenylalanine, β-(α-naphthyl)-β-alanine and N-methyl-β-phenylalanine were taken as objects of investigation. All of these compounds were obtained according to the method of Rodinov [4, 5, 6].

EXPERIMENTAL

β-Phenylalanine [4] was recrystallized twice from water, m.p. 213-214°; β-(α-naphthyl)-β-alanine [5] was washed with ether, m.p. 214-215°; N-methyl-β-phenylalanine [6] was recrystallized from alcohol, m.p. 169°.

Solubility was determined by the gravimetric method. Amino acid excess was treated with water, or with the investigated solution in the flask which was placed in a thermostat at 25 ± 0.1°. The flask was shaken in a special apparatus until equilibrium was reached. Stirring time was determined individually for each amino acid, for which purpose one sample was preheated to 50° and placed in the thermostat, a second sample being placed immediately in the thermostat. Solubility was in good agreement provided shaking was maintained for not less than 35 hours.

Separation of saturated solution from the precipitate was carried out in the thermostat. A pipette was lowered into the flask, on the lower end of which was threaded a funnel into which was sealed a glass filter. The solution was sucked into the pipette and at the same time was filtered. The resulting filtrate was divided into two parts – in one was determined the amino acid concentration, and in the other concentration of hydrogen ions. The sample in which amino acid concentration was determined was weighed in a weighing tube, dried in the oven at 70-90°, and weighed again. Solubility was determined several times in both water and in various hydrogen ion concentrations.

Hydrogen ion concentration was determined by means of a hydrogen electrode. A saturated calomel electrode was used as the reference electrode. The saturated calomel electrode potential was verified before measurement by standarization against the hydrogen electrode immersed in standard acetate buffer solution at pH 4.62.

β-Amino acid solubilities in water at 25° were determined as given in Table 1. Solubility of β-alanine was taken from the literature [1].

TABLE 1

Solubility of β-Amino Acids in Water at 25°

β-Amino acid	Density	Solubility		Number of measurements
		g/100 g of solution	moles/liter	
β-Alanine	1.1581	–	6.125	
β-Phenylalanine	1	1.982	0.1200	5
β-(α-Naphthyl)-β-alanine	1	0.553	0.00226	8
N-Methyl-β-alanine	1.0636	29.625	1.759	3

The resulting data indicate that the carbon chain structure has the greatest effect upon solubility of the β-amino acids. Introduction of a phenyl group into the chain decreases solubility; the solubility of β-phenylalanine is 51-fold less than the solubility of β-alanine. Introduction of the naphthyl radical produces an even greater decrease in solubility. The solubility of α-(α-naphthyl)-β-alanine is 2710-fold less than the solubility of β-alanine. Introduction of an alkyl radical into the amino group has an opposite effect. The solubility of N-methyl-β-phenylalanine is greater than the solubility of β-phenylalanine by 14.6-fold.

The effect of hydrogen ion concentration upon solubility was investigated, using β-(α-naphthyl)-β-alanine as an example. Solutions with various hydrogen ion concentrations were obtained from chemically-pure HCl, with which the amino acid gives a soluble salt.

TABLE 2

Relationship of β-(α-Naphthyl)-β-alanine Solubility to Hydrogen Ion Concentration

Concentration (moles/liter · 10^2)	pH of initial HCl solution	Solubility (S) moles/liter · 10^2)	pH of the saturated solution
0.87	2.06	0.86	2.69
1.269	1.89	1.244	2.47
2.231	1.65	1.518	2.07
4.31	1.37	2.49	1.71
16.10	1.22	2.956	1.49

Dry residue from hydrochloric acid solution was in the form of amino acid hydrochloride. Calculation was made for free amino acid. The experimental results are given in Table 2 and in the Figure.

It can be seen from the data obtained that solubility increases with increase in hydrogen ion concentration. However, there was not observed a simple relation between these values as occurs with some poorly-soluble α-amino acids [7, 8].

It was not possible to determine the solubility of β-(α-naphthyl)-β-alanine in alkaline solutions, since colloidal solutions were formed, difficult to filter, when the pH exceeded 8.

From the pH values for an equimolecular hydrochloride solution of β-(α-naphthyl)-β-alanine and its solubility, it is possible to determine one of its dissociation constants. The resulting constant will express the alkaline dissocation of the NH_2^- group, provided it be assumed that the neutral form of β-amino acid consists of undissociated molecules. If, however, the neutral form of the amino acid is a bipolar ion, then the constant found will characterize the acid properties of the $CO\bar{O}$ group [9]. At present it can be considered to be proved that an aliphatic amino acid exists in aqueous solution in the form of amphoteric ions.

The β-amino acid investigated by the authors was an aliphato-aromatic acid with an amino group in the aliphatic radical. This made it possible to assume that the neutral form in solution is the bipolar ion, similar to amino acids of the aliphatic series. Under this condition, equilibrium in acid solutions of β-(α-naphthyl)-β-alanine hydrochloride can be expressed by the equation:

$$\overset{+}{N}H_3RCOOH \rightleftharpoons \overset{+}{N}H_3RC\bar{O}O + \overset{+}{H},$$

and the dissociation constant by the following ratio:

$$K = \frac{a_H + a_{R\pm}}{a_{R+}}, \qquad (1)$$

where a denotes activity of the corresponding ions.

TABLE 3

Approximate Acid Dissociation Constant for β-(α-Naphthyl)-β-alanine

Amino acid concentration (moles/liter)	HCl concentration (moles/liter)	pH of the saturated solution	pK
0.00866	0.00870	2.69	3.21
0.01242	0.01269	2.47	2.94
0.0223	0.01386	2.07	3.07
0.04312	0.0249	1.71	2.98
0.06100	0.02956	1.49	2.99

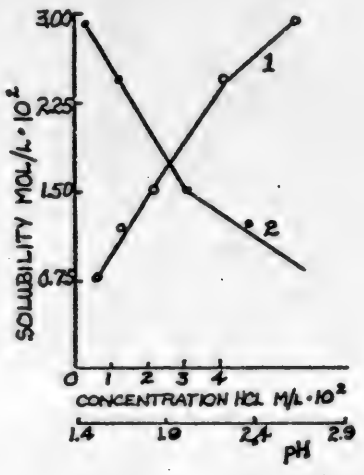
Since the ionizing power of the solutions investigated by the authors is small, it can be considered, therefore, that the ionic activities are equal to their concentrations. Substituting ionic concentration for ionic activity, and introducing the pH value into equation (1), we have:

$$pK = pH - \log \frac{C_{R\pm}}{C_{R+}}. \qquad (2)$$

The values $C_{R\pm}$ and C_{R+} can be readily determined from the following ratios:

$$C_{HCl} = C_{Cl'} = C_{R+} + C_{H+},$$

$$C_{R+} = C_{Cl'} - C_{H+}.$$



Effect of HCl concentration upon the solubility of β-(α-naphthyl)-β-alanine and the relationship of solubility to pH of the saturated solution.

The total amino acid concentration is known from the solubility (S) value at a given pH value. Hence, the concentration of undissociated molecules is equal to $C_{R\pm} = S - C_{R+}$. Substituting the calculated values of $C_{R\pm}$ and C_{R+} into equation (2), there is obtained the pK value. The results are given in Table 3.

As can be seen from the data obtained (Table 3), the pK value deviates sharply for solutions with low hydrochloric acid concentration where salt hydrolysis may be present, but for the other solutions deviations from the average value constitute only about 3%.

SUMMARY

1. The solubilities of β-phenylalanine, β-(α-naphthyl)-β-alanine and N-methyl-β-phenylalanine in water at 25° have been determined.

2. It has been established that introduction of an aromatic radical into the chain lowers the solubility and that introduction of an alkyl radical into the amino group increases the solubility of β-amino acids.

3. The solubility of β-(α-naphthyl)-β-alanine in solutions with varied hydrogen ion concentrations has been determined.

4. The approximate acid dissociation constant for β-(α-naphthyl)-β-alanine has been calculated.

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* See Consultants Bureau Translation, page 1025.

ORIENTATION OF THE TERTIARY-BUTYL GROUP UPON ITS INTRODUCTION INTO THE AROMATIC RING

V. M. Rodionov, V. N. Belov and S. A. Kore

It is known that upon the alkylation of aromatic compounds, the position of alkyl groups entering the ring depends upon the nature of the catalyst used. This generally accepted opinion has been confirmed by the authors' works on introduction of the isopropyl group into cumene. It has been demonstrated that when cumene is alkylated by isopropyl alcohol, the position which the entering alkyl radical takes in the aromatic ring varies, depending upon whether $AlCl_3$ or H_2SO_4 is used [1].

On the other hand an interesting variance from this fact is the butylation reaction of m-xylene. Baur [2], who alkylated m-xylene with isobutyl bromide in the presence of $AlCl_3$, and Noelting [3], who carried out this reaction by reacting isobutyl alcohol with m-xylene in the presence of H_2SO_4, both obtained the same product, namely 1,3-dimethyl-5-tertiary-butylbenzene. It was further demonstrated that the same compound is formed also when using such catalysts as $FeCl_3$, BF_3, and others, in the butylation reaction of m-xylene.

It is of interest to note that similar orientation takes place for the tertiary-butyl group when the secondary-butyl group is introduced into m-xylene in the presence of H_2SO_4, as well as BF_3, forming the 1,3,4-isomer [4].

This fact gives reason for assuming that there is also shown a strong effect by the nature (structure) of the entering alkyl group itself upon orientation of the alkyl group into the benzene ring.

An isomeric hydrocarbon, with substituent positions of 1,3,4, was obtained in the pure state from the organomagnesium compound derived from 1,3-dimethyl-4-iodobenzene and tertiary-butyl chloride [5]. It was shown that 1,3-dimethyl-4-tertiary-butylbenzene reacted with $AlCl_3$ and rearranged into symmetrical dimethyl-tertiary-butylbenzene.

Constants for the isomeric butyl-m-xylenes obtained by various methods are given in Table 1.

TABLE 1

Butyl-m-xylene obtained	Constants			Oxidation products	Literature
	Boiling point (in °)	n_D^{37}	d^{37}		
According to the Grignard reaction	210-214	1.5030	0.9372	Trimellitic acid (1,2,4)	[5]
By butylation of m-xylene with tertiary-butyl chloride in the presence of $AlCl_3$	200-202	1.4890	0.8619	Trimesinic acid (1,3,5)	[5]
By heating the hydrocarbon, obtained according to Grignard, with $AlCl_3$	202-203	1.4903	0.8720	The same	[5]
By butylation of m-xylene with isobutyl alcohol in the presence of H_2SO_4	200-204	–	–	–	[3]
By butylation of m-xylene with isobutylene in the presence of $AlCl_3$	204-206	n_D^{15} 1.4980	d^{15} 0.870	–	[6]

In a work by I. K. Sivkov and coworkers published recently [7], are found brief directions for forming 1,3,5-tertiary-butyl-m-xylene as well as the 1,3,4-isomer from the m-xylene butylation reaction in the presence of H_2SO_4; the effect of H_2SO_4 concentration upon yield of unsymmetrical isomer is noticeable.

However, in none of the cases was the amount of 1,3,4-isomer formed given. Moreover, there was no convincing proof given of the presence of unsymmetrical isomers.

Since the above point is of considerable interest, the authors undertook experimental work for the purpose of clarifying whether or not there is formed any considerable amount of 1,3,4-dimethyl-tertiary-butylbenzene during the butylation reaction of m-xylene with H_2SO_4 present.

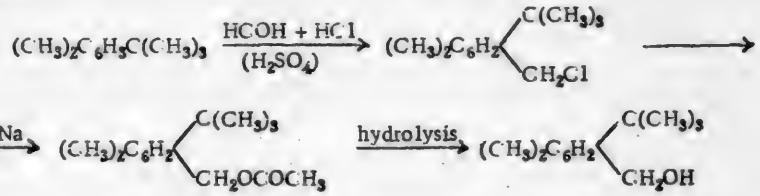
The authors' experiments on butylation of m-xylene with isobutyl alcohol in the presence of H_2SO_4 led to synthesis of 1,3-dimethyl-5-tertiary-butylbenzene, yield of which consitituted about 40% of theory, calculated on the basis of m-xylene entering into reaction, or about 20%, based upon m-xylene taken for reaction (see Table 2 for constants). The unsymmetrical isomer, even if it is formed (which the authors did not prove), is in considerably smaller amount, and can by no means be considered as one of main reaction products.

TABLE 2

Butyl-m-xylene obtained by alkylation of m-xylene in the presence of H_2SO_4	Constants			Melting point (in °)	
	B. p. (in °)	n_D^{20}	d_4^{20}	Trinitro derivative	Corresponding benzyl alcohol
Before heating with $AlCl_3$	204-204.5	1.4962	0.8656	111-112*	98-99**
After heating with $AlCl_3$	203-205	1.4960	0.8665	111-112*	98-99**

The authors did not observe conversion into another isomer upon heating the product obtained by butylation with $AlCl_3$.

Identity of the tertiary-butyl-m-xylene before and after heating with $AlCl_3$ was demonstrated by the authors in preparing the trinitro derivatives and the corresponding trialkyl substituted benzyl alcohols. The latter were prepared according to the scheme:



Constants for the initial hydrocarbons and the hydrocarbons resulting after heating with $AlCl_3$, as well as the constants for these hydrocarbon derivatives, are given in Table 2.

These data indicate that dimethyl-tertiary-butylbenzene obtained by butylation of m-xylene with isobutyl alcohol in the presence of H_2SO_4 does not isomerize upon heating with $AlCl_3$.

Having demonstrated experimentally literature claims to the fact that in the butylation reaction of m-xylene there occurs prefcrentially formation of dimethyl-tertiary-butylbenzene of symmetrical structure, regaidless of the character of the condensing agent used (H_2SO_4 or $AlCl_3$), it appeared of interest to the authors to clarify whether or not it is a general mechanism characteristic for introduction of the tertiary-butyl group into an aromatic hydrocarbon molecule. Certain data on this problem can be found in recently published literature [8] where it is pointed out that introduction of the tertiary-butyl group into the isopropylbenzene molecule in the presence of H_2SO_4 and $FeCl_3$ leads to formation of 1,4-isopropyl-tertiary-butylbenzene as the principal reaction product (0.9 of the total yield), at the same time that introduction of the isopropyl group into the tertiary-butylbenzene under the same conditions forms m- and p-isomers in approximately equal amounts. The authors decided to examine this fact, using as an illustration of butylation, the simplest aromatic hydrocarbon—benzene.

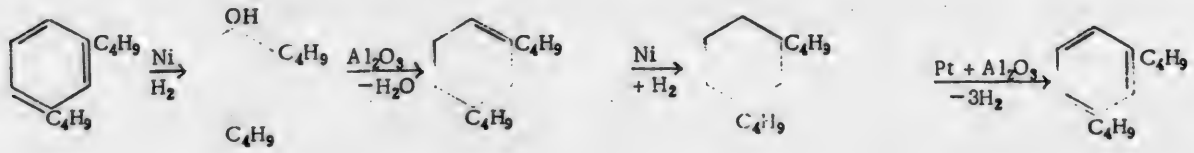
With regard to the structure of dialkyl derivatives which are formed upon butylation of benzene in the presence of $AlCl_3$, there can be found contradictory data in the literature. Introduction of two tertiary-butyl groups into benzene was realized back in the last century by butylation of benzene, both in the presence of $AlCl_3$ [9] and in the presence of H_2SO_4 [10]. In both instances the resulting hydrocarbon was that in which the tertiary butyl groups were found to be in the p-position. Later on, di-tertiarybutylbenzene was synthesized repeatedly by various chemists, via the butylation of benzene in the presence of various catalysts ($AlCl_3$, H_2SO_4, BF_3, HF, $FeCl_3$, P_2O_5, HCl).

There was observed in all cases formation of the p-isomer, with m.p. 76-78°. Only in 1947 did there appear a patent [11] in which, for the first time, there was indicated formation of the m-isomer along with p-di-tertiary-butylbenzene by the alkylation of benzene with isobutylene in the presence of $AlCl_3$. It was indicated in the patent that m-di-tertiarybutylbenzene (for its constants see Table 3) can also be obtained by the isomerization of

* A mixed sample did not give depression upon melting.

** According to the literature data, m.p. of 1,3-dimethyl-5-tertiary-butyl-benzyl alcohol is 99° [4]. Mixed sample on melting did not give depression.

p-di-tertiarybutylbenzene in the presence of $AlCl_3$ with simultaneous passage of hydrogen chloride through the mixture. Other investigators noted later that it was not possible to synthesize m-di-tertiarybutylbenzene by alkylation of benzene with isobutylene. Synthesis of m-di-tertiary-butylbenzene has been realized from 2,4-ditertiarybutylphenol, according to the following equation [12]:



The constants for m-di-tertiarybutylphenol synthesized in such manner coincide with the constants given for the same hydrocarbon in the patent earlier mentioned (Table 3).

TABLE 3

m-Di-tertiarybutylbenzene synthesized	Constants			
	B. p. (in °)	n_D^{20}	d_4^{20}	M. p. (in °)
By alkylation of benzene with isobutylene in the presence of $AlCl_3$ [11]	78.5 at 4.4 mm	1.4870	–	−10.6
From 2,4-di-tertiarybutylphenol	73 at 2.5 mm	1.4879	0.8589	–

In 1951 data were again published, confirming formation of 1,3-di-tertiarybutylbenzene from the alkylation of benzene with isobutylene in the presence of $AlCl_3$ [13].

The authors' experiments on butylation of benzene led only to formation of p-di-tertiarybutylbenzene. Alkylation of benzene was realized by reaction of benzene with isobutyl alcohol in the presence of H_2SO_4, and also with isobutyl chloride in the presence of $AlCl_3$. In both cases there resulted a hydrocarbon of m.p. 77-78°.

A mixed sample of dialkylbenzenes obtained by butylation of benzene in the presence of these two condensing media did not give depression upon melting. Experiments set up by the authors on rearrangement of p-di-tertiarybutylbenzene in the presence of $AlCl_3$ did not lead to formation of m-ditertiarybutylbenzene. The experiments were carried out under various conditions: temperature and reaction were varied. In addition, experiments were carried out with passage of gaseous hydrogen chloride through the reaction. Thus, the indications to be found in the American patent [11] concerning the isomerization of p-di-tertiary-butylbenzene by heating it with $AlCl_3$ have not been confirmed.

The authors' experiments have indicated that the alkylation of benzene by isobutyl alcohol in the presence of H_2SO_4, and with isobutyl chloride in the presence of $AlCl_3$, as well as by heating p-di-tertiarybutylbenzene with $AlCl_3$, do not result in formation of the m-isomer.

This indicates that introduction of the tertiary butyl group into an aromatic hydrocarbon is evidently characterized by the fact that the position of entry of this group is not dependent to any high degree upon the nature of the condensing agent used (H_2SO_4 or $AlCl_3$). There apparently exists in this case the stronger effect of factors which inhibit the orienting effect of a condensing substance.

TABLE 4

Fraction number	B. p. (in °)	n_D^{20}	Quantity (in g)	M. p. of the trinitro derivative (in °)•
1	201-205	1.4960	42	110-111
2	205-210	1.4961	14	112-113
3	210-214	1.4970	3	111-112

It is of interest to mention that upon introducing a tertiarybutyl group into both benzene and m-xylene, there proceeds the formation of symmetrically-composed molecules – in the first instance, of p-ditertiarybutylbenzene, and in the second, of 1,3-dimethyl-5-tertiary-butylbenzene. This characteristic is perhaps, to some degree, connected with the volume taken up by the highly branched tertiary-butyl group.

EXPERIMENTAL

1. Alkylation of m-Xylene by iso-Butyl Alcohol in the Presence of H_2SO_4

Reaction was carried out by the standard procedure for alkylation of aromatic hydrocarbons with alcohols in

• A m.p. of 110° [2] and of 113° [14] has been indicated in the literature for the trinitro derivative of 1,3-dimethyl-5-tertiarybutylbenzene.

the presence of H_2SO_4. 95 g of isobutyl alcohol (b.p. 106-108°) and 278 g of commercial sulfuric acid were taken for 136 g of m-xylene (b.p. 138-139°). After appropriate processing, the reaction product was fractionated at atmospheric pressure. The following fraction resulted from double fractionation (Table 4).

Mixed samples of the trinitro derivatives, from the first and second fractions, melted at 110.5-111.5°; from the second and third fractions – at 111-112°. By further fractionation of the first fraction, the hydrocarbon was isolated: b.p. 204-204.5°; n_D^{20} 1.4962; d_4^{20} 0.8656; MR_D 54.69. $C_{12}H_{18}$. Calculated MR_D 54.015, exaltation ΣMR_D + 0.675; melting point of the trinitro derivative was 111-112°.

This hydrocarbon (35 g) was heated with $AlCl_3$ (7 g) for 3.5 hours on a boiling water bath. After suitable processing and subsequent fractionation, there resulted two fractions: first with b.p. 150-198° in the amount of 7 g, and a second with b.p. 198-207°, in the amount of 18 g. Upon repeated fractionation of the second fraction, a product was isolated (14.5 g) which had:

M.p. 203-205°; n_D^{20} 1.4960; d_4^{20} 0.8665; MR_D 54.61. $C_{12}H_{18}$. Calculated: MR_D 54.015, exaltation ΣMR_D + 0.592; melting point of the trinitro derivative was 111-112°. A sample mixed with the trinitro derivative prepared earlier from the initial hydrocarbon which was not heated with $AlCl_3$, melted at 111-112°.

2. Synthesis of 1,3-Dimethyl-5-tertiary-butylbenzyl Alcohol

50 g of formalin (39.7%) and 79 g of hydrochloric acid (35%) were mixed with 100 g of 1,3-dimethyl-tertiary-butylbenzene (obtained by butylation in the presence of H_2SO_4) and 200 g of commerical hydrochloric acid added at 50° over 1.5 hours. After this, the reaction mass was stirred at 60° for an additional 6 hours. After suitable processing and subsequent vacuum fractionation of the reaction product, there resulted 48 g of fraction containing 98.5% of chloromethyl derivative, which constituted 36.3% of theoretical yield.

B.p. 118-120° (4 mm); n_D^{20} 1.5300; d_4^{20} 1.0084; MR_D 64.51. $C_{13}H_{19}Cl$. Calculated: MR_D 63.50, exaltation ΣMR_D + 1.01.

In addition, there resulted a crystalline product (24 g) of m.p. 134-135°, corresponding to the hydrocarbon di-(2,6-dimethyl-4-tertiary-butylphenyl)methane [15].

Found %: C 89.44, 89.67; H 10.83, 10.83; $C_{25}H_{36}$. Calculated %: C 89.28; H 10.72.

By chloromethylation of dimethyl-tertiary-butylbenzene (30 g) isolated from the hydrocarbon that was heated with $AlCl_3$, there was obtained 17 g of a fraction containing 99.9% of the chloromethyl derivative, which constituted 43.6% of theoretical yield: b.p. 136-137° (11 mm), n_D^{20} 1.5296.

Conversion of the chloromethyl derivative into the corresponding acetoxy derivative was realized in the following manner: 39 g of 1,3-dimethyl-5-tertiary-butyl-benzyl chloride (obtained from the hydrocarbon that was not heated with $AlCl_3$), 25 g of anhydrous sodium acetate and 0.5 g of pyridine were placed into a round-bottomed flask equipped with stirrer, thermometer and reflux condenser. The mixture was heated in such a manner that the temperature would reach 80° during the first hour, and during the next 2 hours would reach 125°. The reaction mass was stirred at this temperature for 4 hours, and then was cooled to 80°; 40-50 g of water was added, and it was stirred again for 30 minutes at 80°. After washing and drying over $CaCl_2$, the reaction product was fractionated in vacuo. The product isolated was in the amount of 29 g, which contained 98.4% of ester, calculating on the basis of 1,3-dimethyl-tertiary-butylbenzyl acetate. The yield of acetate amounted to 67% of theory. The acetate obtained possessed the following constants:•

B.p. 127-129° (2 mm), n_D^{20} 1.5059, d_4^{20} 0.9835, MR_D 70.67. Calculated: MR_D 69.52, exaltation ΣMR_D + 1.15.

Found %: C 77.21, 77.00; H 9.50, 9.36. $C_{15}H_{22}O$. Calculated %: C 76.92; H 9.40.

1,3-Dimethyl-5-tertiary-butylbenzyl acetate was synthesized in similar fashion from the chloromethyl derivative prepared from the hydrocarbon heated with $AlCl_3$. The product contained 98% of the acetate.

The boiling point of the resulting acetate was 151-152° (10 mm), n_D^{20} 1.5064.

Both acetates obtained by saponification with 10% alcoholic NaOH solution gave the same dimethyl-tertiary-butylbenzylic alcohol, with m.p. 98-99° [4]. A sample of the two alcohols when mixed melted at the same temperature.

• There is described in the literature the synthesis of 2,4-dimethyl-6-tertiary-butyl-benzyl acetate by the interaction of dimethyl-tertiary-butylbenzyl chloride, acetic anhydride and acetic acid in the presence of CH_3COOK. However, the constants of the resulting acetate are not given [4].

Found %: C 81.21, 81.23; H 10.66, 10.75. $C_{13}H_{20}O$. Calculated %: C 81.24; H 10.41.

3. Alkylation of Benzene with Isobutyl Alcohol in the Presence of H_2SO_4

1400 g of commercial sulfuric acid was added with stirring to a mixture consisting of 550 g of benzene and 250 g of isobutyl alcohol (b.p. 106-108°) over a period of 1 hour at 60°. Stirring of the mixture was then continued for 6 hours at 70°. The resulting hydrocarbon layer was distilled with steam, a liquid portion distilling off at first (530 g), followed by a crystalline product (115 g). The following fractions were isolated from the liquid portion after repeated fractional distillations:

First fraction 80-110° – 244 g, second fraction 110-166° – 23 g, third fraction, 166-168° – 121 g, and the fourth fraction 168-180° – 53 g. The residue in the flask (20 g) crystallized.

The third fraction had: n_D^{20} 1.4911; d_4^{20} 0.8636, MR_D 44.94. $C_{10}H_{14}$. Calculated: MR_D 44.76.

These constants correspond to literature data for tertiary-butylbenzene [16]. The yield of tertiary-butylbenzene amounted to 31-32% of theory, calculating on the basis of benzene entering into reaction. The crystalline product, recrystallized from ethyl alcohol, had a m.p. of 77-78°, corresponding to di-tertiary-butylbenzene.

Found %: C 88.43, 88.77; H 11.39, 11.61. $C_{14}H_{22}$. Calculated %: C 88.42; H 11.58.

The yield of p-di-tertiary-butylbenzene amounted to 24-25% of theory, calculating on the basis of benzene entering into reaction.

4. Alkylation of Benzene with Isobutylchloride in the Presence of $AlCl_3$

Reaction was carried out under the usual conditions of aromatic hydrocarbon alkylation by alkyl halides in the presence of $AlCl_3$. 20 g of benzene, 16 g of isobutyl chloride (b.p. 67-70°) and 3 g of $AlCl_3$ were taken for reaction. On fractionation of the reaction product (after suitable processing) the following fractions resulted: first fraction 70-100° – 5 g; second fraction 160-210° – 8 g; and third fraction 210-236° – 10 g. By a second distillation of the second fraction, there were isolated from the latter tertiary-butyl benzene (b.p. 166-168°) and a fraction of b.p. 210-220°, from the latter of which, upon cooling, crystallized out a product of m.p. 75-76°.

Similar crystalline products were also isolated by freezing out from the 210-236° b.p. fraction (third fraction). After recrystallization from alcohol, m.p. was 77-78°. A sample mixed with p-di-tertiary-butylbenzene obtained from alkylation of benzene with isobutyl alcohol in the presence of H_2SO_4, melted at the same temperature.

p-Di-tertiary-butyl benzene was heated with $AlCl_3$. The experiments were carried out under various conditions: by heating the mixture on a boiling water bath for 6 hours, and for 4 hours; by heating the mixture at 70-90° for a period of 2-3 hours with simultaneous passage of gaseous hydrogen chloride into the reaction mixture. It should be pointed out that considerable resinification was observed in all experiments. From the reaction products a small amount of liquid product was separated, distilling over a wide range (5 g from 27 g of hydrocarbon taken for reaction, and in another experiment 1 g from 17 g of initial hydrocarbon). By repeated fractionations of the separate fractions, it was possible to isolate a small amount of product with the following constants:*

B.p. 93-98° (10 mm); n_D^{20} 1.4940; d_4^{20} 0.8688; MR_D 63.66. $C_{14}H_{22}$. Calculated: MR_D 63.25.

This product was found to be non-homogeneous. Upon standing, crystals of p-di-tertiary-butylbenzene with m.p. 76-77° precipitated.

SUMMARY

It has been demonstrated that the wide-spread opinion regarding formation of various isomers by alkylation of aromatic hydrocarbons, depending upon the catalyst used ($AlCl_3$ or H_2SO_4) is not justifiable in the case of the tertiary-butyl group introduction into benzene and m-xylene. In these cases there exists a tendency toward formation of symmetrically-composed molecules: 1,3-dimethyl-5-tertiary-butylbenzene in the case of m-xylene butylation, and 1,4-di-tertiary-butylbenzene in the case of benzene butylation.

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* See Consultants Bureau Translation, page 299.

THIOCYANOGENATION OF UNSATURATED COMPOUNDS

I. THIOCYANOGENATION OF UNSATURATED HYDROCARBONS AND OF SILICON-HYDROCARBONS

A. A. Bugorkova, L. N. Petrova and V. M. Rodinov

The similarity in properties of free thiocyanogen with those of the halogens has been the basis for use of thiocyanogen as a reagent for quantitative determination of unsaturated compounds. Free thiocyanogen polymerizes very readily; when dissolved in carbon tetrachloride, chloroform, benzene and carbon disulfide and especially in anhydrous acetic acid, it is relatively stable [1].

The thiocyanogen reaction was first used to determine the extent of acetoacetic ester enolization, and then for determining the degrees of unsaturation of the aliphatic oils of castor, olive, peanut, and others.

A study of the addition of thiocyanogen to oleic, linoleic, linolenic, erucic and brassidic acids has indicated that this reaction proceeds normally [2]. Thus, in the case of linoleic acid, thiocyanogen adds to one of the two ethylenic bonds, and in the case of linolenic acid, to two of the three. Because of this fact, the number of equivalents of thiocyanogen that will add to a given acid does not correspond to the number of bromine equivalents added, when used for analysis of fats and oils.

The feasibility of using thiocyanogen numbers along with iodine and bromine numbers for characterization of unsaturated compounds in other areas of organic chemistry has hardly been touched upon (an exception representing abietinic acid [3]). Only one work is known [4] wherein the author quotes certain data concerning the addition or non-addition of thiocyanogen to a number of compounds which enter into the composition of the ester oils, but no attempt was made to generalize or to clarify the results obtained.

In the study of thiocyanogenation, as an investigative method for ester oils and aromatic substances, the authors tried first of all to apply this procedure to terpene hydrocarbons. Up to the present time there have been no accurate chemical methods for determination of bicyclic hydrocarbons containing one double bond (pinene, carene) in the presence of hydrocarbons containing additional double bonds (dipentene, terpinolene).

The bromination reaction is useless for such purpose since the ring is ruptured by addition of bromine, and the resulting bromine number exceeds considerably the calculated.

It was the authors' assumption that thiocyanogen as a less reactive reagent will not give side-reactions, which was confirmed: α-pinene, β-pinene and Δ^3-carene gave thiocyanogen numbers (Table 1) approximating closely the calculated. Side reactions proceed more slowly with thiocyanogenation than with bromination.

Further investigations have demonstrated that reactivity of the double bond containing a tertiary carbon atom is considerably greater than reactivity of primary and secondary double bonds.

TABLE 1

Addition of Thiocyanogen to Unsaturated Hydrocarbons

Hydrocarbon	Character of the double bond	Percent added			
		Bromine	Thiocyanogen		
		within 5 minutes	within 5 minutes	within 1 hour	within 24 hours
α-Pinene	Tertiary-secondary	246.6	99.7	102.8	157.5
β-Pinene	Tertiary-secondary	227.0	99.3	103.7	151.7
Δ^3-Carene	Tertiary-secondary	146.7	97.9	124.8	135.7
Cyclohexane	Secondary-secondary	98.8	12.9	40.0	96.9
Heptene-1	Primary-secondary	97.7	12.4	36.8	55.0
4,4-Dimethylpentene-1	Primary-secondary	99.3	4.1	23.9	49.4

It can be seen from the data of Table 1 that hydrocarbons having double bonds between the primary and secondary carbon atoms add, within 24 hours, approximately 50% of the calculated quantity of thiocyanogen; within

the same time period, cyclohexene, with a double bond between secondary carbon atoms, adds thiocyanogen completely, and terpene hydrocarbons with double bonds at tertiary carbon atoms add thiocyanogen completely within 5 minutes.

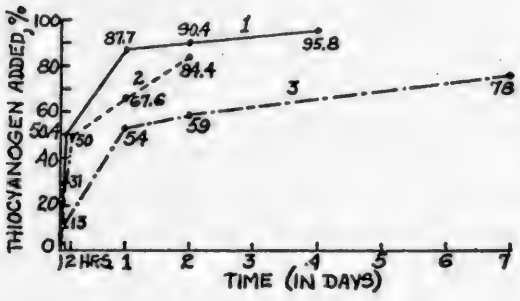
The same pattern was observed by the authors for unsaturated compounds containing functional groups as well.

Results obtained by the authors for bicyclic hydrocarbons gave rise to hope that the thiocyanogen method might offer an opportunity for solving the question of determining them in the presence of hydrocarbons containing two double bonds (for example, limonene in the presence of pinene). It was found, however, that limonene reacts quite rapidly with one molecule of thiocyanogen, and exceptionally slow with the other Complete addition of thiocyanogen to limonene is attained only after 96 hours.

With the example of limonene, there was also studied in greater detail 2,10-dimethyl-dodecadiene, as well as diallyl, and the same phenomenon of predominant addition of thiocyanogen to one of the two bonds of diolefinic compounds was observed, as up to the present time has been observed only with linoleic acid.

In order to solve the problem of whether in actuality the addition of thiocyanogen to one double bond inhibits thiocyanogenation of the second bond, the authors investigated the behavior of diallyl —a hydrocarbon with two identical bonds.

Within the first 25 hours one of the double bonds of diallyl added thiocyanogen completely; however, addition to the second bond proceeded only 56% in 7 days. The diallyl thiocyanogenated product obtained during that period corresponding to addition of one thiocyanogen molecule only, and having, according to the authors' assumption, the structure $CH_2(SCN)CH(SCN)CH_2CH_2CH{=}CH_2$, was a heavy, red-brown liquid, and contained 13.97% N (for $C_8H_{10}S_2N_2$ Calculated %: N 14.1).



Quantity of thiocyanogen added, in % of theory. 1) Limonene; 2) dimethyldodecadiene; 3) diallyl.

The double bond of the substance isolated reacted with bromine very rapidly (similarly to that of diallyl), and added thiocyanogen very slowly.

Upon prolonged thiocyanogenation with a solution of higher concentration, the authors succeeded in isolating diallyl tetrathiocyanogen $CH_2(SCN)CH(SCN)CH_2CH_2CH(SCN)CH_2(SCN)$ —a yellow crystalline compound, m.p. 168° (with decomposition).

By combining data of the authors with data of the literature, a deduction can be made that compounds containing two double bonds add thiocyanogen at one bond with considerably greater rapidity than at the second bond.

In determining unsaturation of organosilicon compounds, the bromination reaction does not always give satisfactory results.

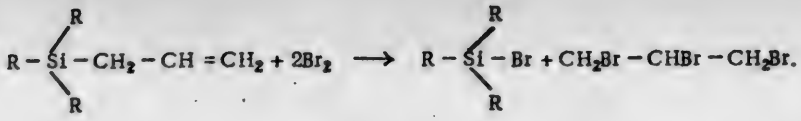
After studying the thiocyanogen addition to double bonds of unsaturated compounds containing silicon, the authors determined that the presence of silicon promotes addition of thiocyanogen, which can be explained on the basis of a higher positive silicon charge.

Silicon hydrocarbons containing a double bond between primary and secondary carbon atoms are considerably more reactive than hydrocarbons of similar structure which do not contain silicon. Particularly clear-cut is the effect of silicon upon addition of thiocyanogen to a double bond in position 2,3. Monoallyl derivatives, as can be seen in Table 2, react almost immediately with the thiocyanogen molecule, although the character of the remaining three radicals bound to silicon also has some effect upon the addition rate.

If two or three allyl groups are present in the silicon hydrocarbon molecule, then their various bonds, in contrast to the olefinic hydrocarbons, will react with thiocyanogen independently of one another. However, the reaction rate decreases somewhat in proportion to the increase in number of allyl groups.

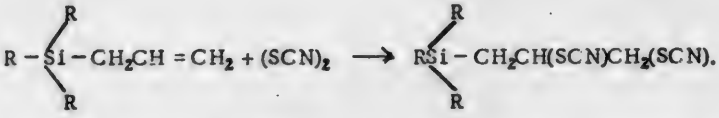
Rearrangement of the double bond in silicon hydrocarbons to positions 3,4 and 4,5 slows down the addition of thiocyanogen somewhat, to that approximating analogous aliphatic hydrocarbons.

When reacting bromine with unsaturated silicon hydrocarbons, there occurs addition of excessive amounts of bromine (as compared with the calculated), due to rupture of the molecule [5].

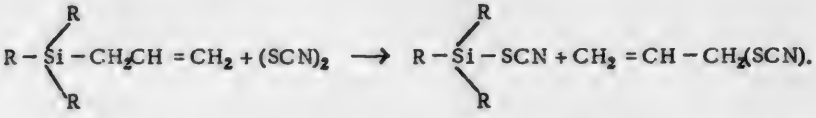


It has been determined by the authors that for thiocyanogenation of each double bond of a silicon hydrocarbon, there is consumed exactly one molecule of thiocyanogen.

The thiocyanogenation reaction can proceed either in the direction of addition at the double bond of thiocyanogen,



or in the direction of rupture of the silicon hydrocarbon without subsequent addition of thiocyanogen at the double bond,



In order to illustrate the problem of direction of the reaction, the authors isolated a product resulting on reaction of thiocyanogen with triallylethylsilane. The resulting product was a solid crystalline material containing nitrogen in amount corresponding to the composition $C_{17}H_{20}SiS_6N_6$.

This fact makes it possible to assume that thiocyanogenation of unsaturated silicon hydrocarbons proceeds in the direction of double bond addition.

TABLE 2

Thiocyanogen Addition to Unsaturated Silicon Hydrocarbons

Silicon hydrocarbon	Percent thiocyanogenation within		
	5 minutes	1 hour	24 hours
Trimethylallylsilane	93.3	93.9	–
Triethylallylsilane	96.4	96.4	–
Tripropylallylsilane	92.2	97.3	–
Triethylisobutenylsilane	97.2	99.3	–
Methyldiallylsilane	76.8	93.7	–
Methyltriallylsilane	81.6	95.6	–
Trimethylbutenylsilane	6.9	37.7	99.6
Triethylmethylpentenylsilane	5.2	31.2	93.0
Dimethylphenylmethylpentenylsilane	13.8	24.1	96.2

The unsaturated silicon hydrocarbons were submitted by V. F. Mironov; for their syntheses and properties, see [8].

EXPERIMENTAL

The solution of free thiocyanogen was prepared by action of bromine upon lead thiocyanate in anhydrous acetic acid [6].

The experimental data are given in Table 3, where, in the first column, are enumerated substances used for the investigation, with indications for their methods of synthesis and their properties.

Synthesis of diallyl dithiocyanide. 1 g of diallyl was treated with 250 ml of thiocyanogen solution in glacial acetic acid (1: 6). The acetic acid was neutralized after 24 hours with sodium carbonate to the appearance of an

TABLE 3

Names and properties of the compounds used in the investigation	Calculated thiocyanogen or bromine number	Time	Weighed portion (in g)	Thiocyanogen number found	Percent of theory
α-Pinene: b.p. 20-21° (1 mm); n_D^{20} 1.4660; d_4^{20} 0.8580; bromine number (5 min.) 246.6	117.25	5 min.	0.0940	117.0	99.7
		1 hour	0.1030	120.6	102.8
		24 hours	0.0732	184.8	157.5
β-Pinene: b.p. 161-162°; n_D^{20} 1.4754; d_4^{20} 0.8720; bromine number (5 min.) 227.0	117.25	5 min.	0.1088	116.5	99.3
		1 hour	0.1008	121.7	103.7
		24 hours	0.1055	168.5	143.6
Δ^3-Carene: b.p. 167-169°; n_D^{20} 1.4720; d_4^{20} 0.8640; bromine number (5 min.) 192.3	117.25	5 min.	0.0966	114.3	97.4
		1 hour	0.0740	146.4	124.8
		24 hours	0.0648	159.3	135.8
Cyclohexene: b.p. 83°; n_D^{20} 1.4450; d_4^{20} 0.8198; bromine number 192.3	194.5	5 min.	0.1084	25.2	12.9
		1 hour	0.1141	77.9	40.05
		24 hours	0.1095	188.5	96.9
Heptene-1 was obtained by decomposition of heptyl acetate by passage over glass chips at 475°: b.p. 93-94°; d_4^{20} 0.7020; n_D^{20} 1.4004; bromine number 159.5	162.8	5 min.	0.1001	20.2	12.4
		1 hour	0.1062	60.1	36.8
		24 hours	0.0950	89.8	55.0
4,4-Dimethylpentene-1: b.p. 71-72°; n_D^{20} 1.3925; d_4^{20} 0.6991; bromine number (5 min.) 161.6	162.8	5 min.	0.0744	6.68	4.1
		1 hour	0.0773	38.9	23.9
		24 hours	0.0826	80.5	49.4
Limonene: b.p. 62-63° (12 mm); n_D^{20} 1.4732; d_4^{20} 0.8440; bromine number (5 min.) 236.3	234.6	5 min.	0.1066	71.07	30.3
		1 hour	0.0842	118.2	50.4
		24 hours	0.0707	206.2	87.7
		2 days	0.0802	212.0	90.4
		4 days	0.0809	224.4	95.8
Diallyl was obtained according to the Grignard reaction [7]: b.p. 58-58.2° (744 mm); n_D^{20} 1.4012; d_4^{20} 0.6873; bromine number (5 min.) 389.3	389.2	5 min.	0.0933	0	0
		1 hour	0.0788	51.6	13.3
		24 hours	0.0631	210.2	54.0
		2 days	0.0554	231.05	59.4
		4 days	0.0668	266.35	68.4
		7 days	0.0735	305.1	78.4
2,10-Dimethyldodecadiene: b.p. 239-240°; n_D^{20} 1.4453; d_4^{20} 0.7930; bromine number (5 min.) 159.2	164.5	5 min.	0.0987	9.7	5.9
		1 hour	0.1015	51.2	31.1
		2 hours	0.0980	82.3	50.0
		24 hours	0.0926	113.5	67.6
		2 days	0.0924	139.4	84.4

oily layer. The oil was extracted with ether. After removal of ether from the ether extract, which was dried beforehand over calcium chloride, a red-brown oil remained, possessing an unpleasant odor, readily soluble in alcohol. The product was purified to remove resins by boiling with carbon. After removal of the alcohol, a dark-yellow oil remained.

Found %: N 13.97. $C_8H_{10}S_2N_2$. Calculated %: N 14.12.

Thiocyanogen number. Found: After 24 hours, 43.0; after 48 hours, 61.76. Calculated as diallyl dithiocyanide: 80.8

Synthesis of a completely thiocyanogenated diallyl product. 570 ml of 0.2 N thiocyanogen solution in glacial acetic acid (1: 15) was added to 1 g of diallyl. The reaction mixture was left for one week. After completion of reaction, there settled out to the bottom a precipitate of yellow flakes which dissolved upon shaking the flakes and passing through a filter. The solution was neutralized to a weakly acid reaction and the precipitate was filtered off. The reaction product was in the form of a yellow precipitate, insoluble in water, alcohol, ethyl acetate, acetic acid, and poorly soluble in chloroform.

After recrystallization from chloroform, there resulted yellow crystals which melted at 167-169° (with decomposition), which did not add thiocyanogen.

Found %: N 17.38. $C_{10}H_{10}S_4N_4$. Calculated %: N 17.8

SUMMARY

1. The thiocyanogen addition reaction differs greatly from the addition reaction of halogens, first of all in its selectivity.

2. Thiocyanogenation permits determination of double bonds in those compounds which, under the action of bromine, give side reactions, and for which determination of bromine numbers is impossible (bicyclic terpene hydrocarbons and unsaturated hydrocarbons).

3. The extent of application of thiocyanogen numbers for quantitative determination purposes is limited to the unsaturated compounds for which reaction goes completely within a practical time period – not more than 24 hours. The thiocyanogen reaction is not suitable for determination of hydrocarbons containing primary-secondary double bonds.

4. In the case of limonene, diallyl and dimethyldodecadiene, addition of thiocyanogen proceeds at one double bond, inhibiting further thiocyanogenation.

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Substances

THIOCYANOGENATION OF UNSATURATED COMPOUNDS

II. EFFECT OF OXYGEN-CONTAINING FUNCTIONAL GROUPS UPON THE THIOCYANOGENATION REACTION

A. A. Bugorkova, L. N. Petrova and V. M. Rodionov

The presence of oxygen-containing functional groups modifies considerably reactivity of the double bond. It has been determined by the authors that the presence, near the double bond, of carbinol, as well as of the carbonyl and carboxyl groups, inhibits the thiocyanogenation reaction.

Data are given in Table 1 for thiocyanogenation of unsaturated alcohols, aldehydes, ketones, carboxylic acids and their derivatives, with differently situated double bonds. As can be seen from these data, the presence of a carbinol group in position 1,2 (allyl alcohol, cinnamyl alcohol) lowers considerably reactivity of the double bond. In the case of the unsaturated alcohols, methylallylcarbinol and diallylcarbinol, in which the double bond is in the 2,3-position relative to the carbinol group, the latter showing hardly any noticeable effect, their rate of thiocyanogenation approximates the thiocyanogenation rate of the corresponding hydrocarbons.

Citronellol and geraniol add thiocyanogen quite rapidly at the double bond between tertiary and secondary carbon atoms, the second double bond of geraniol not adding at all, apparently under the influence of both the carbinol group and thiocyanogen group which has been added at the more distant bond.

As the result of a study of the bromine and thiocyanogen numbers for geraniol and citronellol, which are of great importance in production of aromatic substances, the authors have succeeded in developing a method for separate determination of them in mixtures containing a saturated alcohol. The total number of double bonds in the unsaturated alcohols is determined by bromination, and the number of double bonds at a distance from the carbinol group – by thiocyanogenation. The difference between resulting bromine and thiocyanogen numbers indicates the geraniol content.

The aldehyde group displays a decelerating action which approximates that of its action upon the carboxyl group. Aldehydes with a double bond in position 1,2–cinnamic, amylcinnamic, and others – do not add thiocyanogen at all.

With 2,6-dimethylhepten –3-al-1, having a double bond in the 2,3-position, there is observed a slow addition of thiocyanogen.

Citronellal and citral with double bonds in the 5,6-position add thiocyanogen quite rapidly. Citral, however, adds thiocyanogen only at the far double bond.

It is known from the literature that the presence of a carboxyl group lowers considerably reactivity of the double bond in relation to a number of reactants, the halogens in particular. It was found that the bromine addition reaction depends upon position of the double bond relative to the carboxyl group. Thus, for example, for crotonic acid $K = 1.8\text{-}2.4 \cdot 10^{-5}$, and for allylacetic $K = 1.4\text{-}2.3 \cdot 10^{2}$ [1].

This effect, relative to thiocyanogen, is especially large. If effect of the carbinol group disappears upon rearrangement of the double bond at the β,γ-position, then, as can be seen from the table, the effect of the carboxyl group is extended over the more remote double bonds.

The double bond in position 1,2 to the carboxyl group, as can be seen in the case of nonylenic acid and of cinnamic acid, does not add thiocyanogen at all. Butene and octahydro-β-naphthylacetic acid which have double bond in the 2,3-position hardly add thiocyanogen.

Following rearrangement of the double bond to the 3,4-position, the effect of the carboxyl group decreases: pentenic acid reacts in the same fashion as the corresponding unsaturated hydrocarbon with similar double bond.

TABLE 1

Addition of Thiocyanogen to Unsaturated Alcohols, Aldehydes, Ketones and Carboxylic Acids

Name	Percent thiocyanogenation within the time			Double bonds position relative to the functional group
	5 min.	1 hour	24 hours	
Alcohols				
Allyl alcohol	1.0	9.5	19.4	1.2
Cinnamic alcohol	1.6	6.7	19.3	1.2
Methylallyl carbinol	1.4	10.5	60.2	2.3
Diallylcarbinol	1.2	11.45	54.2	2.3
Citronellol	93.2	99.6	100.1	5.6
Geraniol	46.3	50.8	51.7	5.6 (1.2)
	92.6	101.7	100.4•	
Aldehydes				
Cinnamic aldehyde	0	0	0	1.2
α-Amylcinnamic aldehyde	0	0	0	1.2
α-Methyl-p-isopropylcinnamic aldehyde	0	0	1.4	1.2
2,6-Dimethylhepten-3-al-1	0	2.2	20.2	2.3
Citronellal	85	100.0	100.2	5.6
Citral	35.8	50.2	51.8	5.6 (1.2)
Acids and their Derivatives				
Nonylenic acid	0	0	1.8	1.2
Cinnamic acid	0	0	0	1.2
Methyl ester of Nonylenic acid	0	0	1.6	1.2
Acrylic acid nitrile	0	0	0	1.2
Butenic acid	1.2	2.4	6.9	2.3
Octahydro-β-naphthylacetic acid	–	2.2	9.2	2.3
Pentenic acid	0.7	5.7	53.2	3.4
Citronellic acid	87.5	95.5	98.4	5.6
Geranic acid	30.1	43.0	50.0	5.6 (1.2)
Nitrile of geranic acid	31.7	47.9	50.9	5.6 (1.2)
Petroselinic acid	34.6	30.8	99.4	5.6
Ketones				
Mesityl oxide	2.2	3.2	14.2	(1.2)
2-Methylhepten-4-one-6	1.8	3.5	6.4	(1.2)
Benzalacetone	0	0	5.7	1.2
β-Ionone	0	4.0	22.7•	2.4
Methylionone	6.4	15.1	35.2•	–
Isomethylionone (iralia)	5.2	11.5	24.5•	–
α-Ionone	0	1.7	6.2•	–
Isopulegone	10.9	31.0	96.5	–
Carvone	2.9	12.6	58.6••	–
6-Methylhepten-5-one-2	162	170	177.2	–
Allylacetone	5.8	26.2	110.1	–
Pseudoionone	98.5	103.1	108.2•	–
Isomethylpseudoionone	99	102.1	116.2	–

• Thiocyanogen addition takes place at one double bond.

•• Calculated for one double bond.

With petroselinic and citronellic acids possessing the same remote position of double bond (position 5,6) the character of the bond is already markedly evident. Petroselinic acid, having a double bond between the secondary carbon atoms, adds about 35% thiocyanogen within 5 minutes, and citronellic acid, with a double bond between the tertiary and secondary carbon atoms, within the same time period adds 87% of thiocyanogen, by calculation.

TABLE 2

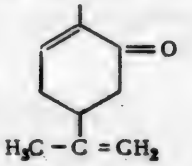
Thiocyanogenation of Unsaturated Alcohols

Names and properties of substances used for the thiocyanogenation study	Theoretical thiocyanogen or bromine number	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Allyl alcohol: b.p. 96°; n_D^{20} 1.4139; d_4^{20} 0.8545; bromine number 276.0	275.2	5 min.	0.0887	2.7	0.98
		1 hour	0.1061	26.3	9.56
		24 hours	0.1045	53.6	19.47
Cinnamic alcohol: b.p. 129-131° (4 mm); m.p. 32.5-33°; bromine number 118.1	119.1	5 min.	0.1106	1.87	1.57
		1 hour	0.1193	7.96	6.7
		24 hours	0.1015	23.02	19.33
Methylallylcarbinol: Obtained by the Grignard reaction [2]: b.p. 120-121°; d_4^{20} 0.8440; bromine number 176.0	185.6	5 min.	0.1135	2.7	1.4
		1 hour	0.1035	19.4	10.5
		24 hours	0.0871	112.3	60.2
Citronellol: b.p. 98° (3 mm); n_D^{20} 1.4583; d_4^{20} 0.8635; bromine number 101.4	102.3	5 min.	0.0674	95.31	93.17
		1 hour	0.0878	101.95	99.67
		24 hours	0.0724	102.4	100.1
Geraniol: Purified as the calcium chloride compound; b.p. 102-104° (4 mm); n_D^{20} 1.4775; d_4^{20} 0.8835; alcohol content (by acetylation) 99.3%; bromine number 206.9	207.3	5 min.	0.0996	96.0	92.6
		0.5 hour	0.1091	102.3	98.7
		1 hour	0.0894	105.4	101.7
		24 hours	0.0926	107.2	103.4
Diallylcarbinol: Obtained by the Grignard reaction from the ethyl ester of formic acid and allyl chloride; b.p. 151.5-152.5°; d_4^{20} 0.8634; alcohol content (according to the Zerevitinoff method) 98.5%	284.5	5 min.	0.0808	3.36	1.18
		1 hour	0.0859	32.6	11.4
		24 hours	0.0665	154.35	54.2

Geranic acid adds thiocyanogen quite rapidly at the double bond farther removed, and does not add at its double bond which is in the 1,2-position. A study of the addition of thiocyanogen to unsaturated acid derivatives – acrylonitrile, the nitrile of geranic acid, the diallyl ester of maleic acid, and others – indicates that the mechanism found for the free acids is also maintained by their derivatives.

As in the case of other oxygen-containing groups, the ketone group which is in the 1,2-position relative to the double bond inhibits addition of thiocyanogen. α,β-Unsaturated ketones – 6-methylhepren-3-one-2, benzalacetone, mesityl oxide – add thiocyanogen hardly at all. Ketones with conjugated double bonds in the α,β-position to the keto group: pseudoionone $(CH_3)_2C=CHCH_2CH_2\underset{\displaystyle CH_3}{\overset{|}{C}}=CHCH=CHCOCH_3$ and isomethylpseudoione $(CH_3)_2C=CHCH_2CH_2\underset{\displaystyle CH_3}{\overset{|}{C}}=CH-CH=\underset{\displaystyle CH_3}{\overset{|}{C}}COCH_3$, as to be expected, add thiocyanogen only at the remote double bond; for ketones with a double bond more remote from the keto group, the thiocyanogenation reaction ceases to conform to the general rules as determined for compounds of other classes.

For the two ketones, carvone and isopulegone, having identical structures, differing only in the double bond position relative to the keto group, carvone



should have added thiocyanogen at the remote double bond more rapidly than isopulegone

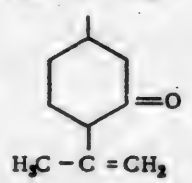


TABLE 3

Thiocyanogenation of Unsaturated Aldehydes

Names and properties of substances used for the thiocyanogenation study	Theoretical thiocyanogen or bromine number	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Cinnamic aldehyde: b.p. 121° (6 mm); n_D^{20} 1.620; aldehyde content (by oximation) 100.2%; bromine number 120.3	120.9	5 min.	0.1181	0	0
		1 hour	0.1025	0	0
		24 hours	0.1002	0	0
α-Methyl-p-isopropylcinnamic aldehyde: b.p. 151-152° (12 mm); n_D^{20} 1.5810; d_4^{20} 0.9901; aldehyde content (by oximation) 98.2%.	84.9	5 min.	0.1012	2.4	2.8*
		1 hour	0.1115	3.5	4.2
		24 hours	0.1032	3.9	4.6
α-Amylcinnamic aldehyde: b.p. 138-139° (6 mm); n_D^{20} 1.5501; d_4^{20} 0.9646; aldehyde content (by oximation) 98.7%; bromine number 77.4	78.9	5 min.	0.1105	0	0
		1 hour	0.1080	0	0
		24 hours	0.1127	2.1	2.7
2,6-Dimethylhepten-3-al-1: obtained from the glycide ester [3]; b.p. 52-55° (2 mm); n_D^{20} 1.4500; d_4^{20} 0.8712; aldehyde content (by oximation) 98.3%; bromine number 107.5	114.0	5 min.	0.1219	0	0
		1 hour	0.0972	2.5	2.2
		24 hours	0.1073	23.1	20.2
Citronellal: b.p. 102° (10 mm); d_4^{20} 0.8551; aldehyde content (by oximation) 99.4%; bromine number 102.9	103.6	5 min.	0.1179	88.2	85.1
		1 hour	0.1088	102.9	99.4
		24 hours	0.0993	102.3	98.7
Citral: b.p. 103° (10 mm); n_D^{20} 1.4880; d_4^{20} 0.8882; aldehyde content (by oximation) 100.2%; bromine number 208.4	210.0	5 min.	0.1293	74.2	35.4
		1 hour	0.1163	103.2	49.1
		24 hours	0.1033	106.1	52.5

The double bond of carvone, which is situated at the 1,2-position, does not add thiocyanogen, and its presence should not affect reactivity of the double bond. It can be seen from the Table data, however, that isopulegone adds one molecule of thiocyanogen completely within 24 hours, while carvone adds only 59%.

The cause for such strange behavior of unsaturated ketones is to be sought for not only in the negative effect of the keto group upon the thiocyanogenation of the double bond, but also in the possibility of side reactions. One of the causes which may complicate thiocyanogenation of the double bond may be the formation of the enolic form of the ketone and addition of thiocyanogen at the enolic double bond. Methylheptenone with a double bond in the same position as carvone, adds thiocyanogen very rapidly in an amount exceeding 100%, no doubt due to rapid formation of the enolic form.

Apparently, addition of thiocyanogen to isopulegone also, is explainable not by addition at the usual double bond, but at the double bond of the enol form. Carvone, which is less prone to enolization, adds thiocyanogen more slowly at the enolic double bond. However, addition at the usual double bond for carvone, isopulegone and α-ionone is probably inhibited by presence of the keto group.

The above-indicated situation does not allow collection of clear-cut data on thiocyanogenation of unsaturated ketones; however, in some cases, the thiocyanogen numbers can be used to analyze unsaturated ketones. Thus, pseudoionone and pseudoisomethylionone – intermediate products in the synthesis of such aromatic substances as ionone and methylionone – react quantitatively quite readily with thiocyanogen, whereas the cyclic products of their isomerization – ionone and isomethylionone – almost fail to react at all with thiocyanogen; therefore, the method of determining thiocyanogen numbers can be used for the study and control of the pseudoionone and methylpseudoionone isomerization to the corresponding cyclic ketones.

EXPERIMENTAL

The conditions for thiocyanogenation and for the preparation of free thiocyanogen solution are given in the preceding article.

* Negligible thiocyanogen number found, which did not increase with increase in reaction time, no doubt explicable by the presence of impurities of an unsaturated nature.

TABLE 4

Thiocyanogenation of Unsaturated Acids and Their Derivatives

Names and properties of substances used for the thiocyanogenation study	Theoretical thiocyanogen or bromine number	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Nonylenic acid: b.p. 95-97° (5 mm); acid content 100.3%; bromine number (0.2 N bromine solution) 100.25.	102.3	5 min.	0.1065	0	0
		1 hour	0.0984	0	0
		24 hours	0.1077	1.89	1.8
Methyl ester of nonylenic acid: b.p. 92-93° (8 mm); ester number 328.4; bromine number 91.7	93.89	5 min.	0.0942	0	0
		1 hour	0.1065	0	0
		24 hours	0.0949	1.7	1.8
Cinnamic acid: m.p. 132.5°; acid content 97.5%; bromine number 104.9	107.85	5 min.	0.1106	0	0
		1 hour	0.0956	0	0
		24 hours	0.1037	0	0
Acrylic acid nitrile: b.p. 78°	301.2	5 min.	0.0891	0	0
		1 hour		0	0
		24 hours		0	0
Butenic acid: Obtained according to Grignard from allyl iodide and carbon dioxide [4]: b.p. 163-164°; n_D^{20} 1.4260; acid content 91.1%; bromine number 81.5	185.6	5 min.	0.0900	2.2	1.2
		1 hour	0.0931	4.48	2.4
		24 hours	0.0971	12.9	6.9
Octahydro-β-naphthylacetic acid: b.p. 172-174°; (9 mm); m.p. 81-82°; acid content 99.1%; bromine number 81.5	82.25	5 min.	0.0985	0	0
		1 hour	0.0979	1.8	2.2
		24 hours	0.1025	7.6	9.2
Pentenic acid: Obtained from the diethyl ester of allylmalonic acid; b.p. 78° (4 mm); n_D^{20} 1.4310; acid content 99.2%; bromine number 159.1	159.6	5 min.	0.0979	1.07	0.7
		1 hour	0.1099	9.2	5.7
		24 hours	0.0995	84.9	53.2
Petroselenic acid: Obtained by saponification of coriander oil: m.p. 31-32°; acid content 99.1%; bromine number 56.3	56.59	5 min.	0.0990	19.56	34.6
		1 hour	0.0920	51.4	90.8
		24 hours	0.1013	56.23	99.4
Citronellic acid: Obtained by oxidation of citronellal with silver oxide [5]: b.p. 150-151° (17 mm); n_D^{20} 1.4545; acid content 100.1%; bromine number 94.3	94.45	5 min.	0.1358	82.4	87.5
		1 hour	0.1282	90.17	95.5
		24 hours	0.9908	92.9	98.4
Geranic acid: Obtained by saponification of geranic acid nitrile; b.p. 118-119° (20 mm); d_4^{20} 0.9518; acid content 98.6%; bromine number: (5 min) 95.3; (24 hours) 188.2	190.2	5 min.	0.0936	57.3	30.1
		1 hour	0.1037	81.7	43.0
		24 hours	0.0908	95.1	50.0

The experimental data are presented in Tables 2-5, in the first columns of which are indicated the preparative method and the properties of the substances used for the thiocyanogenation study.

Method for Analysis of Geraniol-Citronellol-Isodecyl Alcohol Mixture

Thiocyanogen solution and bromine solution according to Kaufmann were added, respectively, to weighed samples, from 0.05 to 0.1 g, of the investigated mixture, and two parallel control experiments set up. 1 Hour following addition of 10 ml of 10% potassium iodide solution, the bromine excess and the thiocyanogen were titrated with 0.1 N thiosulfate solution, and the bromine and thiocyanogen numbers for the mixture determined.

Designating the difference between the bromine and thiocyanogen numbers for the mixture as A, the percent geraniol, x, is found from the ratio: $x = \frac{100A}{104}$, where: 104 - difference between the thiocyanogen and bromine numbers of geraniol and citronellol; the percent citronellol, y, is determined according to the formula: $y = \frac{e \cdot 100 - 208 \cdot x}{104}$, where: e = bromine number, x = percent geraniol, and 104 = bromine number of citronellol.

TABLE 5

Thiocyanogenation of Unsaturated Ketones

Names and properties of substances used for the thiocyanogenation study	Theoretical thiocyanogen or bromine number	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Benzalacetone: b.p. 128° (9 mm); m.p. 42°; bromine number (1 hour) 125.5	109.3	5 min.	0.1089	0	0
		1 hour	0.1044	0	0
		24 hours	0.1156	6.2	5.7
Mesityl oxide: b.p. 128-129° (745 mm); d_4^{20} 0.8582; n_D^{20} 1.4441; bromine number 196.8 (1 hour).	162.8	5 min.	0.0990	3.2	2.2
		1 hour	0.1013	5.3	3.2
		24 hours	0.0976	23.1	14.2
6-Methyl-3-hepten-2-one: Obtained by condensation of isovaleric aldehyde with acetone in alkaline medium [6]: b.p. 60-63° (8 mm); n_D^{20} 1.4422; d_4^{20} 0.8510; ketone content (by oximation) 98.0%	126.7	5 min.	0.1031	2.4	1.8
		1 hour	0.1100	4.4	3.5
		24 hours	0.1116	8.1	6.4
β-Ionone: b.p. 76-80° (0.1 mm); n_D^{20} 1.5204; d_4^{20} 0.9446; ketone content (by oximation) 98.9%; m.p. of semicarbazone 148-149°	83.1	5 min.	0.1139	0	0
		1 hour	0.1012	3.3	4.0
		24 hours	0.1057	18.5	22.7
Methylionone: b.p. 127-128° (10 mm); n_D^{20} 1.5004	77.5	5 min.	0.0970	4.9	6.4
		1 hour	0.1058	11.6	15.1
		24 hours	0.1080	27.2	35.2
α-Isomethylionone (iralia): b.p. 120-121° (8 mm); n_D^{20} 1.5001; d_4^{20} 0.9312	77.5	5 min.	0.0987	4.1	5.2
		1 hour	0.1008	8.9	11.15
		24 hours	0.0933	19.0	24.5
α-Ionone: b.p. 120-121° (10 mm); n_D^{20} 1.4989; d_4^{20} 0.9308; ketone content (by oximation) 99.1%; m.p. of semicarbazone 136-137°	83.1	5 min.	0.0975	0	0
		1 hour	0.1130	1.4	1.7
		24 hours	0.1296	5.2	6.2
Isopulegone: Obtained by oxidation of isopulegol [7] prepared by heating citronellal with acetic anhydride: b.p. 83-84° (9 mm); n_D^{20} 1.4670; d_4^{20} 0.9193; ketone content (by oximation) 99.2%; bromine number 132.2	105.0	5 min.	0.0979	11.4	10.9
		1 hour	0.0937	32.6	31.0
		24 hours	0.0948	101.35	96.5
Carvone: Isolated from caraway oil; b.p. 114-115° (8 mm); n_D^{20} 1.4992; d_4^{20} 0.9614	106.4	5 min.	0.1048	3.05	2.9
		1 hour	0.1013	13.4	12.6
		24 hours	0.1185	62.4	58.6
6-Methylhepten-5-one-2: Obtained by heating citral with an aqueous solution of potash; b.p. 89° (8 mm); n_D^{20} 1.4400; d_4^{20} 0.8602; ketone content (by oximation) 99.1%; bromine number 203.4	126.7	5 min.	0.1127	204.4	162.0
		1 hour	0.0934	215.1	170.0
		24 hours	0.0999	223.6	177.2
Allylacetone: Obtained by saponification of allylacetoacetic ester [8] with barium hydroxide: b.p. 128-129°; d_4^{20} 0.8469; ketone content (by oximation) 98.3%; bromine number 128.6	162.8	5 min.	0.1003	9.5	5.8
		1 hour	0.1026	43.7	26.8
		24 hours	0.1037	179.3	110.1
Pseudoionone: b.p. 128-130° (10 mm); n_D^{20} 1.5332; d_4^{20} 0.8978	83.1	5 min.	0.1085	81.8	98.5
		1 hour	0.1008	85.7	103
		24 hours	0.1170	95.0	108.2
Isomethylpseudoionone: b.p. 140-141° (10 mm); n_D^{20} 1.5221	77.5	5 min.	0.0952	76.6	99.0
		1 hour	0.0979	79.1	102.1
		24 hours	0.1173	89.9	116.2

The quantity of saturated compounds is determined as the difference between $x + y$ and 100%.

Example. Geraniol, citronellol and isodecyl alcohol mixture has a bromine number of 93.84 and a thiocyanogen number of 36.64. Hence, the composition of the mixture (in %) = geraniol 5.5; citronellol 80.6; isodecyl alcohol 14.5%.

SUMMARY

1. The presence of oxygen-containing functional groups (alcohol, aldehyde, ketone and carboxyl) lowers the ability of the double bond to react with thiocyanogen. The enumerated functional groups display an unusually strong effect on a double bond in the 1,2-position, to which thiocyanogen hardly adds. There is scarcely any effect of functional groups upon double bonds in the 3,4-position and further.

2. The addition reaction of thiocyanogen to unsaturated ketones is complicated by addition of thiocyanogen to the enolic form of a ketone.

3. A method for individual determinations of geraniol and citronellol in a mixture with saturated alcohol has been given.

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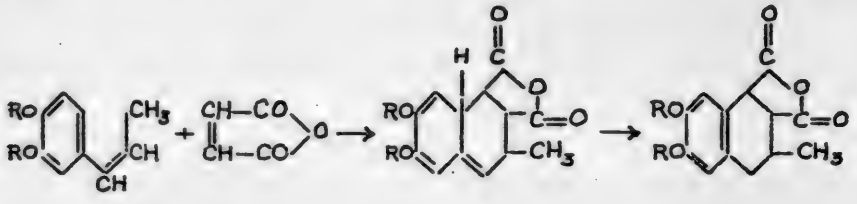
THIOCYANOGENATION OF UNSATURATED COMPOUNDS

III. THIOCYANOGENATION OF THE DOUBLE BOND SIDE CHAIN OF METHOXY- AND METHYLENEDIHYDROXY- COMPOUNDS OF THE AROMATIC SERIES

A. A. Bugorkova, L. N. Petrova and V. M. Rodionov

Aromatic compounds possessing a side allyl or propenyl group (anethole, methylchavicol, safrole, isosafrole, eugenol and isoeugenol) play a considerable role in the chemistry of perfumery materials. The bromine number method not only fails to allow separate determinations of allyl and propenyl compounds, but in some cases is also unsuited for the analysis of individual compounds because of side reactions involving replacement of nuclear hydrogen. The authors have established that introduction of the methoxy- and of the methylenedihydroxy- groups into the aromatic nucleus of related compounds increases sharply reactivity of the double bond conjugated with the phenyl radical, relative to addition of thiocyanogen, i.e., with the propenyl compounds anethole, isosafrole and isoeugenol thiocyanogenation occurs quantitatively within 5 minutes. Compounds with an allyl side chain – such as the methoxy or methylenedihydroxy group contained in the ring (safrole, eugenol), as well as those that do not contain them (allylbenzene, propenylbenzene) – react with thiocyanogen very slowly (Table 1).

There are indications in the literature concerning a characteristic behavior of double bonds of the aromatic series which are conjugated with a double bond in the side chain and are under the influence of the methoxy and methylenedihydroxy groups. Isosafrole and methylisoeugenol, as with compounds containing a conjugated system of double bonds, give with maleic anhydride a product which rearranges into a tetrahydronaphthalene derivative [1]:



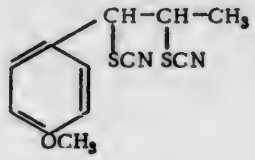
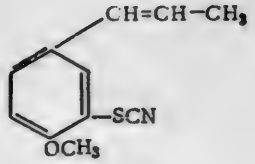
Anethole gives a normal addition product containing two molecules of maleic anhydride, i.e., it reacts as a compound with two conjugated double bond systems [2].

Data obtained by the authors on thiocyanogenation have confirmed that aromatic bonds in such methoxy- and methylenehydroxy- compounds lose their aromatic character and assume a state of conjugation with the double bond of the side chain, thus increasing reactivity of the latter.

Influence of the methoxy and methylenedihydroxy groups is also evident in reactivity of the side chain double bond which is under the negative influence of oxygen-containing functional groups.

It can be seen from data of the same table that benzalacetone and cinnamic acid do not react at all with thiocyanogen, while at the same time anisalacetone reacts quantitatively within 24 hours. p-Methoxycinnamic acid and piperonylacrylic acids add, within 24 hours, 34 and 19% respectively, of thiocyanogen.

In order to elucidate whether in actuality addition of thiocyanogen proceeds at the double bond under the authors' conditions, and not by substitution, the authors isolated the anethole thiocyanogenation product, which can be represented as:

either  or 

The anethole thiocyanogenation product separated by the authors contained nitrogen in an amount corresponding to the addition product. (10.06% nitrogen was found. For $C_{12}H_{12}OS_2N_2$ it was calculated to be 10.6).

A different concept toward thiocyanogenation of methoxylated allyl and propenyl compounds made it possible to solve the problem of individual determination of isosafrole in the presence of safrole, and isoeugenol in the presence of eugenol.

The feasibility of such determinations was demonstrated on a series of synthetically prepared mixtures, the analytical results for which are given in the experimental part.

TABLE 1

Name	Percent thiocyanogenation within the given time		
	5 minutes	1 hour	24 hours
Allylbenzene	–	2.4	58.3
Propenylbenzene	2.3	7.7	59.0
Anethole	98.8	99.4	100.2
Safrole	1.5	14.6	82.6
Isosafrole	99.9	100.6	–
Eugenol	3.7	26.0	–
Isoeugenol	98.3	99.8	101.6
Benzalacetone	–	–	5.7
Anisalacetone	2.4	20.7	100
Cinnamic acid	–	–	–
p-Methoxycinnamic acid	–	3.8	34.1
Piperonylacrylic acid	–	2.1	18.9

EXPERIMENTAL

For preparation of free thiocyanogen, see Article I. Characterizations of the investigated compounds and their thiocyanogen numbers are presented in Table 2.

Method of Determination

A weighed sample of about 0.1 g of the substance to be investigated was placed into a dry, ground-glass stoppered flask. 20 ml of thiocyanogen was added by automatic pipette. After 5 minutes, 10 ml of 10% potassium iodide solution was added to the flask, and the separated iodine titrated with 0.1 N hyposulfite solution. A parallel control experiment was carried out at the same time.

TABLE 2

Name, structure and properties of the products investigated	Bromine or thiocyanogen number, calcd.	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Allylbenzene: b.p. 156-157° b.p. 156-157°; n_D^{20} 1.5151; d_4^{20} 0.8931	135.2	5 minutes	0.1020	0	0
		1 hour	0.1007	3.18	2.4
		24 hours	0.1055	78.8	58.3
Propenylbenzene was obtained by isomerization of allylbenzene: b.p. 171°; n_D^{20} 1.5485; d_4^{20} 0.9142	135.2	5 minutes	0.1064	3.2	2.3
		1 hour	0.1002	10.4	7.7
		24 hours	0.1011	79.8	59.0
Anethole was isolated from fenchilic acid: b.p. 112-113° (9 mm); m.p. 22-22.5°	107.2	5 minutes	0.1024	106.5	98.8
		1 hour	0.1023	107.2	99.4
		24 hours	0.0962	108.1	100.2
Safrole: b.p. 99-100° (7 mm); n_D^{20} 1.5370; freezing point 11°	98.2	5 minutes	0.0973	1.48	1.5
		1 hour	0.1098	14.4	14.6
		24 hours	0.1065	81.4	82.6
Isosafrole: b.p. 103.5-104° (3 mm); n_D^{20} 1.5773	98.52	5 minutes	0.0971	98.45	99.9
		30 minutes	0.1096	98.4	99.4
		1 hour	0.1119	99.16	100.6

(Table continued on next page)

TABLE 2 (continued)

Name, structure and properties of the products investigated	Bromine or thiocyanogen number, calcd.	Time	Sample weight (in g)	Thiocyanogen number found	Percent of theory
Eugenol was isolated from oil of eugenol basil: b.p. 124° (9 mm); n_D^{20} 1.5420; d_4^{20} 1.0702	97.3	5 minutes	0.1215	3.2	3.7
		1 hour	0.0950	25.4	26.0
		24 hours	0.1071	92.6	95.2
Isoeugenol b.p. 132° (8 mm); m.p. 16°	97.3	5 minutes	0.1104	95.6	98.5
		1 hour	0.1008	97.1	99.8
		24 hours	0.1084	98.9	101.6
Benzalacetone: b.p. 128° (9 mm); m.p. 42°: ketone content (by oximation) was 99.2%	109.3	5 minutes	0.1089	0	0
		1 hour	0.1044	0	0
		24 hours	0.1156	6.2	5.7
Anisalacetone: m.p. 73-73.5°; ketone content (by oximation) was 99.0%	92.8	5 minutes	0.1161	2.2	2.4
		1 hour	0.1208	19.2	20.7
		24 hours	0.1076	92.9	100
Cinnamic acid: b.p. 132.5°, percent content by acid number 97.5; bromine number (24 hours) 104.9	107.8	5 minutes	0.1106	0	0
		1 hour	0.0966	0	0
		24 hours	0.1037	0	0
p-Methoxycinnamic acid was obtained by condensation of anise aldehyde with malonic acid in pyridine medium [2]; m.p. 188°	89.8	5 minutes	0.1012	0	0
		1 hour	0.0974	3.45	3.8
		24 hours	0.1413	30.6	34.1
Piperonylacrylic acid: m.p. 238°	90.7	5 minutes	0.1210	0	0
		1 hour	0.1293	1.9	2.1
		24 hours	0.1118	17.2	18.9

The percent isoeugenol isosafrole and anethole (A) was calculated according to the formula

$$A = \frac{80(a-b)}{sT_{calc.}}$$

where a = quantity of 0.1 N hyposulfite solution used in titration of the control; b = titration of weighed sample; s = weighed sample of substance investigated; $T_{calc.}$ = calculated thiocyanogen number.

TABLE 3

Analysis of a Synthetic Mixture of Safrole-Isosafrole

Quantity of isosafrole (in %)	Calculated thiocyanogen number	Found thiocyanogen number				Found isosafrole (in %)			
		I	II	III	average	I	II	III	average
78.9	77.4	77.9	77.13	77.92	77.46	78.87	78.38	78.47	78.6
48.1	47.3	47.55	48.18	47.62	47.78	48.32	48.8	48.33	48.48
23.18	22.8	23.82	23.8	23.78	23.8	23.79	24.2	24.1	24.03
14.27	14.06	14.57	14.60	14.73	14.6	14.81	14.84	14.97	14.82
11.9	11.71	12.3	12.21	12.2	12.43	12.5	12.41	12.38	12.43

TABLE 4

Analysis of a Synthetic Mixture of Eugenole-Isoeugenole

Amount of isoeugenol (in %)	Calculated thiocyanogen number	Found thiocyanogen number	Found isoeugenol (in %)
90.5	88.1	88.58	91.0
75.0	73.0	73.2	75.2
71.6	69.7	70.2	72.1
48.3	47.0	47.54	48.8
19.95	19.4	20.8	21.3

SUMMARY

1. Introduction of the methoxy and methylenedihydroxy groups into an aromatic ring affects thiocyanogen addition to the double bond in the side-chain which is conjugated with the double bond of the aromatic ring.

2. A method for quantitative determination of the propenyl group in the presence of the allyl group in an aromatic compound, which contains in the ring a methoxy or methlenedihydroxy group, has been given: for isosafrole in the presence of safrole, and for isoeugenol in the presence of eugenol .

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INTERMEDIATE PRODUCTS FOR SYNTHESIS OF AROMATIC SUBSTANCES

I. SYNTHESIS OF 1,14-TETRADECANDICARBOXYLIC ACID

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E. K. Smolyaninova and V. N. Belov

The synthesis of α,ω-dicarboxylic acids of the aliphatic series, containing 14-18 carbon atoms in the chain, offers formidable difficulties. The most convenient synthetic method for these compounds is apparently the electrolysis of the acid ester salts of α,ω-carboxylic acids of a simpler composition [1]. Recently mention was made of the synthesis by condensation of α,ω-dihalo derivatives with two molecules of acetoacetic ester, and its rupture to form the corresponding diketone [2].

There has also been developed recently a synthetic method for monosubstituted acetoacetates by direct alkylation of sodium acetoacetate resulting from the condensation of ethyl acetate (without intermediate separation of the free acetoacetate) [3]. In the present work, the authors have used this method for synthesis of the diethyl ester of 2,13-diacetyl-1,14-tetradecandicarboxylic acid (I), which was then converted into 1,14-tetradecandicarboxylic acid (II).

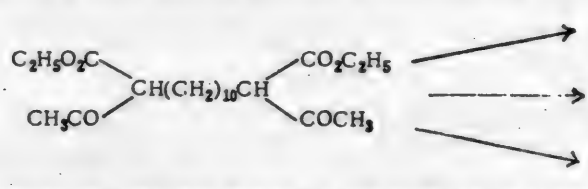
$$C_2H_5O_2CCH_2(COCH_3) + Br(CH_2)_{10}Br + CH_2(COCH_3)CO_2C_2H_5 \longrightarrow C_2H_5O_2CCH(COCH_3)-(CH_2)_{10}-CH(COCH_3)CO_2C_2H_5$$

$$C_2H_5O_2CCH(COCH_3)(CH_2)_{10}CH(COCH_3)CO_2C_2H_5 \longrightarrow HOOCCH_2(CH_2)_{10}CH_2COOH$$

(I) (II)

Synthesis of (I) was carried out by heating 1,10-dibromodecane mixture with the condensation product of ethyl acetate (carried out in the presence of dry sodium ethylate) under conditions analogous to that described earlier for synthesis of monosubstituted acetoacetates [3]. However, in the given instance, the alkylation product (I) was not isolated in pure form since attempts to fractionate the reaction mixture (after suitable processing) resulted in extensive resinification. After distilling off excess ethyl acetate and unreacted acetoacetate from the reaction mixture (treated in the proper manner), a product resulted having: acid number 6.5-8.5; ester number 280-290; the bromine content 1-3%; oximation data corresponding to that of (I), 79-85%. This product underwent rupture.

During the process of selecting conditions for the acid split (I), the authors noted that upon heating with rather strong alkali solution, splitting occurred in both directions (the ketone split and the acid split):



$HO_2CCH_2(CH_2)_{10}CH_2CO_2H$ (II)

$HO_2CCH_2(CH_2)_{10}CH_2COCH_3$ (IV)

$CH_3COCH_2(CH_2)_{10}CH_2COCH_3$ (III)

It was found that heating with 15, and even as high as 33%, potassium hydroxide solution, led for the most part to the formation of hexadecan-2,15-dione (III). The diacid (II) under such conditions was formed only in small amount. Evidently keto acid (IV) was formed as well, during the splitting reactions, from a molecule of the diacetyl derivative of the diacid (I).

It was possible to obtain the diacid (II) in satisfactory yield only by using potassium hydroxide and water in a weight ratio of 5:1. In this case, the main product having been isolated from the reaction mixture after a single recrystallization from aqueous alcohol (1:1), had a m.p. of 112-116° and represented, according to the analytical data (determination of the acid number and the keto group), 80-85% diacid (II) in admixture with 20-15% keto acid (IV). The yield of diacid amounted to about 60% of theory, calculating on the basis of dibromodecane taken for the condensation reaction. After purification with diethyl ether, the diacid (II) melted at 122-123°; keto acid

was not present, and it was possible only in some cases to detect a negligible amount. Such purification accounted for the losses: yield (II) constituted 30-33%, also calculating on the basis of dibromodecane.

EXPERIMENTAL

330 g of the reaction mixture*, obtained by condensation of ethyl acetate in the presence of dry sodium ethylate with 45 g of dibromodecane (m.p. 43-44°) was placed in a 750 ml flask, equipped with thermometer, mercury seal and stirrer. The reaction mixture was stirred thoroughly, maintaining a temperature of 78-80° for 40-45 hours, treated with 200 ml of water (to complete dissolution of precipitate) and the upper layer which separated was washed with a solution of sodium chloride to the point of neutral reaction.

After distilling off the excess ethyl acetate, the unreacted acetoacetate was removed under vacuo. The residue, amounting to 58-62 g (its characterization being given in the general section) underwent acid splitting. For this purpose, 150 g of finely-powdered potassium hydroxide and 30 ml of water were placed in a 750 ml flask equipped with stirrer and dropping funnel. The flask was immersed in an oil bath in such manner that the level of the reaction mixture was somewhat lower than that of the oil level in the bath (in order to avoid crystallization of the reaction product upon the cold walls of the flask). At a temperature of 95-100°, the condensation product (I) was added to alkali dropwise over a period of 1 hour, without allowing temperature to exceed 110°. The reaction mixture was then heated at the same temperature for about 2 more hours. By that time, the reaction mixture had solidified considerably, and after cooling to room temperature, was almost solid. The flask contents were treated with 500 ml of water and then acidified with hydrochloric acid (1:1) to an acid reaction with Congo red. The crystallized product (II) which resulted was filtered with suction and dried to constant weight at a temperature of 50-60°. There resulted 35-37 g of diacid (II) which was contaminated with resinous impurities and which contained a certain amount of keto acid (IV). The product was dissolved in hot 50% alcohol, in which a portion of the impurities was insoluble. The solution was decanted onto the filter. The resulting transparent solution, upon cooling, precipitated as crystals (II) of m.p. 114-116°; acid number was 370-380. According to oxidation data, the keto acid (IV) content was about 15%. The yield was 23.2 g or about 60% of theory, calculating on the basis of initial dibromodecane. After recrystallization from the alcohol, m.p. was 123-124°.**

Found %: C 65.30; H 10.45. Acid number 430. $C_{15}H_{26}O_4$. Calculated %: C 65.08; H 10.14. Acid number 434.

The keto acid (IV) isolated from the reaction mixture had a m.p. of 75-76°.

Found %: C 70.39; H 11.11. Acid number 214.1. $C_{15}H_{28}O_3$. Calculated %: C 70.27; H 11.01. Acid number 218.7.

Purification of (II) can be effected by its conversion to the dimethyl ester. A mixture of 17.5 g of technical (II), 22 g of methyl alcohol, and 4 g of concentrated H_2SO_4 was left at room temperature. After 2-3 days, crystals of the dimethyl ester separated, and were distilled in vacuo. There resulted 7.8 g of the dimethyl ester with b.p. 185-188° (at 6 mm); after recrystallization from alcohol, m.p. 42.5-43.5°.*** On saponification of the ester, there resulted acid (II) with m.p. 122-123°; yield was almost quantitative.

SUMMARY

It has been demonstrated that 2,13-diacetyl-1,14-tetradecandioic acid can be obtained by the interaction of 1,10-dibromodecane with the condensation product of ethyl acetate in the presence of dry sodium ethylate.

For the additional conversion into 1,14-tetradecandioic acid, the 2,13-diacetyl-1,14-tetradecandioic acid can be used in the crude form.

By carrying out the splitting reaction under very rigorous conditions (weight ratio of KOH to water = 5:1), there results the diacid containing about 15% of keto acid, from which separation can be effected by recrystallization. However, if 15 or 33% KOH solution is used, the principal product of rupture is found to be the hexadecane-2,15-dione.

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* This amount corresponds to 0.50-0.55 mole of sodium ethylate used for condensation.

** According to the literature data: m.p. 123° [4]; 124° [5].

*** According to the literature data, m.p. 41° [5].

[2] M. Stoll, A. Rouve, Helv. Chim. Acta, 30, 2019 (1947); M. Stoll, op. cit., 34, 1820 (1951).

[3] V. M. Rodionov, V. N. Belov, E. A. Agorodnilova and N. N. Shevyakova, Works of the All-Union Research Institute of Synthetic and Natural Aromatic Substances, Vol. I, 5 (1952).

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All-Union Research Institute of Synthetic and Natural Aromatic Substances.

INTERMEDIATE PRODUCTS FOR SYNTHESIS OF AROMATIC SUBSTANCES

II. HEXADECANE-2,15-DIONE SYNTHESIS

V. M. Rodionov, N. E. Kologivova, E. A. Ogorodnikova and V. N. Belov

In the preceding article [1] which described conditions for synthesis of 1,14-tetradecandioic acid by acid splitting of the condensation product between dibromodecane and two molecules of acetoacetic ester, it was observed that in addition to the acid split, there also occurred in practically all instances the ketone split, leading to formation of the corresponding keto acid and hexadecane-2,15-dione.

Data have been given for synthesis of hexadecane-2,15-dione by rupture of the above-mentioned condensation product with alcoholic potassium hydroxide solution at room temperature for 5 days [2, 3]. The yield of product, m.p. 83-84°, according to the data was 30% of theory.

Because of the fact that this diketone is an intermediate in the synthesis of certain macrocyclic ketones [4, 5], the authors carried out a series of experiments which had as their object the task of finding conditions for securing maximum yield of hexadecane-2,15-dione in the reaction indicated. Rupture of the condensation product indicated above was carried out in acid, alkaline and neutral media. The reaction time and the concentrations of reactants were varied in separate experiments. As a result of the work carried out, it was established that by heating in an acetic acid medium of varying concentration (up to that of glacial acetic acid), the product did not undergo change. Using sodium hydroxide in the concentration range 2 to 33%, ketonic rupture proceeded rapidly, leading to the formation of diketone in good yield (see Experimental). Hexadecane-2,15-dione was also formed by heating the condensation product in an autoclave with water for 5 hours at a temperature of 200°. In this case, however, the process was accompanied by considerable resinification.

EXPERIMENTAL

The best results were obtained by carrying out the reaction in the following manner. 29 g of the dibromodecane condensation product with acetoacetic ester, prepared according to the method indicated in article I [1], 120 ml of alcohol, and a 10% aqueous solution of sodium hydroxide were placed in a 200 ml flask equipped with reflux condenser, and the total heated for 1 hour. The diketone formed by cooling the reaction mixture crystallized, which was easily separated. 13.2 g of crystalline product resulted, with m.p. 70-75°.

TABLE

Quantity of condensation product taken (in g)*	Concentration of NaOH or CH_3COOH	Reaction time (in hours)	Quantity of resulting diketone (in g)	Melting point of the diketone (in °C)	Yield of diketone (in % of theory recalculated to dibromodecane)
10.0	25 g 10% aqueous NaOH	1	2.6	81-82.5	40.6
10.0	25 g 10% aqueous NaOH	3	2.59	80-82	40.4
10.0	25 g 10% aqueous NaOH	0.5	1.2	83-84	18.7
5.0	68 g 2% aqueous NaOH	1	0.68	81-83	21
10.0	40 g 10% CH_3COOH	1	Initial product isolated unchanged		
10.0	40 g 10% CH_3COOH	6			
10.0	30 ml glacial acetic acid	1			
10.0	50 g 5% aqueous alcoholic NaOH	1	2.42	80-82	37.7
10.0	40 g 10% aqueous alcoholic NaOH	1	2.85	80-82	53.8
10.0	20 ml water	5 at 200°	3.3	71-75	62 (Resinous product)

* The product prepared under the conditions described earlier was used.

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Yield amounted to 71% recalculated to dibromodecane taken for the condensation reaction. After double recrystallization from aqueous alcohol (1: 1), the hexadecane-2,15-dione had a m.p. of 85-86° which remained unchanged upon additional recrystallizations. Yield of recrystallized diketone constituted about 50% of theory, calculating again on the basis of dibromodecane.

Found %: C 75.24, 75.45; H 11.85, 11.82. $C_{16}H_{30}O_2$. Calculated %: C 75.54; H 11.88%.

Semicarbazone m.p. 198-199°. According to the literature data [3], m.p. 199-200°.

Results of experiments under other conditions are given in the Table.

SUMMARY

On rupture of the condensation product of 1,10-dibromodecane with two molecules of acetoacetic ester with 10% aqueous-alcoholic solution of sodium hydroxide, there results hexadecane-2,15-dione in yield up to 71% of theory (calculating on the basis of dibromodecane taken for condensation). Yield of pure product with m.p. 85-86° constitutes about 50% of theory.

Under such conditions no products of acid cleavage are formed.

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[2] M. Stoll, A. Rouve, Helv. Chim. Acta, 30, 2019 (1947).

[3] M. Stoll, Helv. Chim. Acta, 34, 1817 (1951).

[4] M. Stoll, U. S. patent 2526171 (1950).

[5] Julian W. Hill, U. S. patent 2556876 (1951).

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• See Consultants Bureau Translation, page 1927.

NEW DATA ON THE PROBLEM OF γ-CHLOROACETOACETIC ESTER CONDENSATION AND THE SYNTHESIS OF δ-CHLOROLEVULINIC ACID

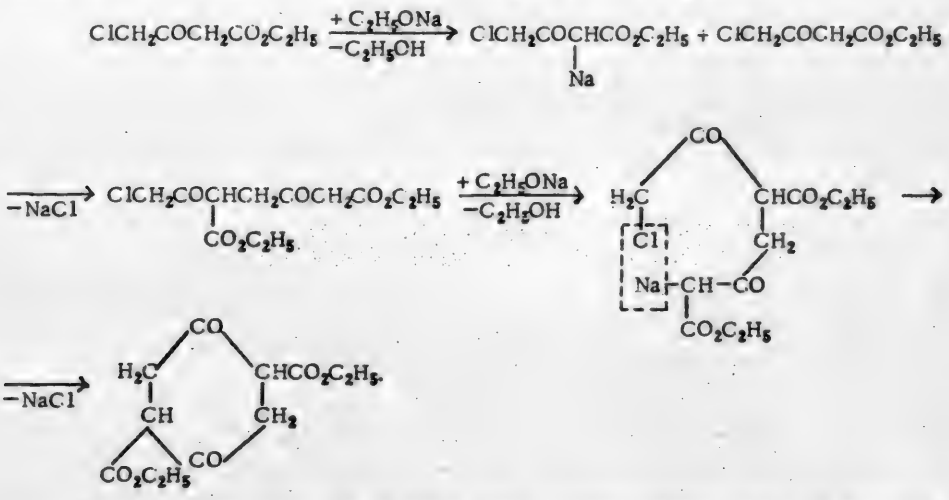
V. M. Rodionov and M. A. Gubareva

The purpose of this investigation was preparation of δ-chlorolevulinic acid, which is not described in the literature. This latter compound can be used as the starting material for synthesis of certain important amidazole derivatives of histidine, histamine, and other types.

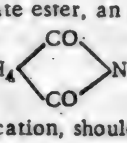
Of the halogenated levulinic acid derivatives β-chloro- and β-bromo-levulinic acids prepared by interacting levulinic ester with the corresponding halides are known, as well as the α- and β-bromolevulinic acids, prepared by the addition of hydrogen bromide to acetylacrylic acid, and by bromination of α-angelicolactone [1]. X-Monochlorolevulinic acid, so-called [2], synthesized by reaction of phosphorus pentachloride with levulinic acid, was found, so far as can be assumed from the excessive chlorine content and liquid state of the reaction product, to be a mixture of the monochlorolevulinic acid with some disubstituted product.

Since levulinic acid is readily obtained by condensation of acetoacetic and monochloroacetic esters [3], an attempt was made to prepare δ-chlorolevulinic acid by interacting γ-chloroacetoacetic ester with the monohalogenated acetate prepared according to the procedure described by Rodionov and Polunina [4]. The γ-chloroacetoacetic ester necessary for condensation was prepared according to the excellent procedure of Aleksandrov, by reacting magnesium with chloroacetic ester [5].

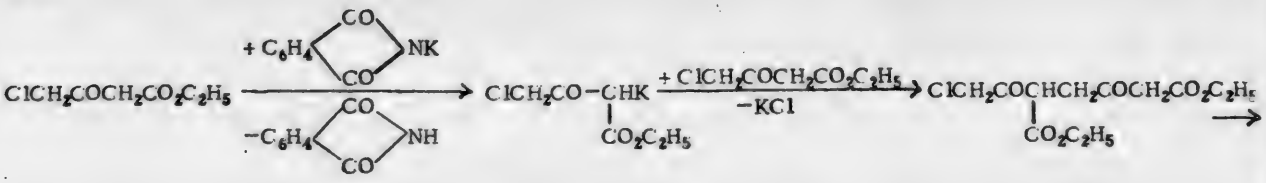
By carrying out condensation of chloroacetoacetic ester with chloroacetic ester in the presence of sodium ethylate, a nicely-crystallizing compound was isolated with m.p. 127°, plus a large amount of viscous, considerably resinified oil. Upon investigation, the crystalline substance was found to be the succinic ester. The same product resulted by similar treatment of γ-chloroacetoacetic ester without chloroacetic ester. This implied that the condensation reaction apparently proceeds according to the following scheme:

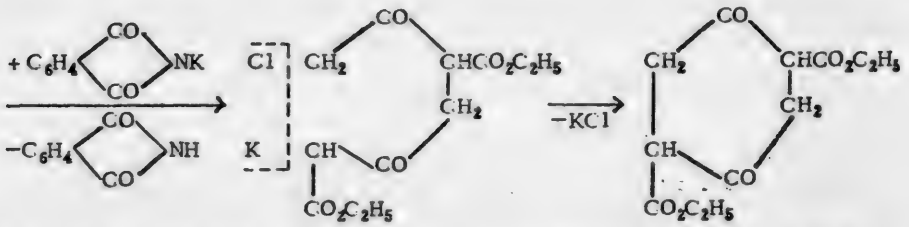


The succinyl succinate ester obtained from γ-chloroacetoacetic ester did not differ, according to its elementary analysis, its molecular weight, and other properties, from the compound described earlier in the literature [6].

In addition, in order to avoid formation of succinylsuccinate ester, an attempt was made to replace the chlorine of γ-chloroacetoacetic ester by the phthalylamino group  . Phthalylaminoacetoacetic ester, upon condensing with chloroacetic ester and subsequent saponification, should have given δ-aminolevulinic acid. However, upon reacting potassium phthalimide with γ-chloroacetoacetic ester, there also occurred formation of

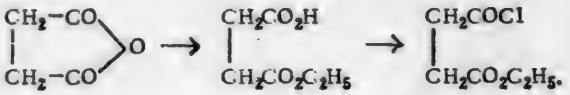
succinylsuccinate ester. Thus, potassium phthalimide in the given case was found to function only as a condensing agent.





The succinylsuccinate ester resulting after purification possessed a m.p. of 127.5°. Yield was 56.4% of theory. A sample mixed with the product of the preceding synthesis did not give depression in melting point.

In addition, the δ-chlorolevulinic acid needed by the authors was obtained in high yield (90% of theory) according to the method of Arndt-Eistert [7]. For this purpose, succinic acid, through its anhydride, was converted into this acid ester and into its chloroanhydride:



The monochloroanhydride gave diazoketone with diazomethane, converting into the δ-chlorolevulinic acid ester when reacted with hydrogen chloride.

$$ClCOCH_2CH_2CO_2C_2H_5 + CH_2N_2 \rightarrow N_2CHCOCH_2CH_2CO_2C_2H_5 \xrightarrow{HCl} ClCH_2COCH_2CH_2CO_2C_2H_5.$$

The mechanism of these reactions without question attests to the presence of chlorine in the molecule of chlorolevulinic ethyl ester, located in the δ position, and does not give reason to expect simultaneous formation of other isomers. The diazomethane necessary for synthesis was prepared from hydrazine hydrate, chloroform and potassium hydroxide [8].

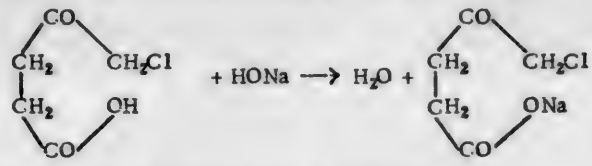
The ethyl ester of 4-diazo-3-butanoncarboxylic acid obtained in the second step of the process was a pleasant-smelling, mobile oil. The ethyl ester of δ-chlorolevulinic acid, which resulted from the latter when reacted with hydrogen chloride, was found to be a colorless, mobile liquid with an ethereal odor; corrosive action upon the skin, especially upon the mucous membrane of the eye. Analytical data for chlorine, as well as values for molecular refraction of the compound, were in good agreement with the formula $C_7H_{11}O_3Cl$.

The δ-chlorolevulinic acid, quantitatively isolated from the ester, represented colorless crystals, m.p. 72.5-73.5°, readily soluble in water and acetic acid, less so in benzene and alcohol, very poorly so in ether, chloroform and carbon tetrachloride. The elementary analysis, chlorine analysis, as well as titration data for determination of the equivalent weight for the acid, confirmed the formula $C_5H_7O_3Cl$. The δ-chlorolevulinic acid was also characterized through its semicarbazone, m.p. 148-149°.

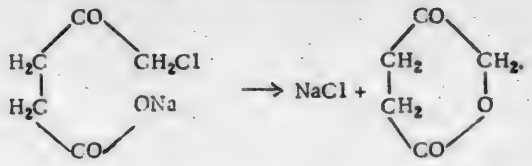
Upon studying the properties of δ-chlorolevulinic acid, it was found that the salts and amide cannot be isolated from it. Thus, upon neutralization of alcoholic and aqueous solutions of the acid with dilute solutions of alkalies and soda, upon evaporation, the mineral salts were produced instead of δ-chlorolevulinic acid salt—chlorides—and an oil which did not possess acid properties, and evidently represented the lactone of δ-hydroxylevulinic acid.

It should be considered that rupture of the chloride, with formation of the heterocyclic compound, occurs only with heating and evaporation, since only after heating of the neutral solution does silver nitrate give a precipitate of silver chloride. The reaction course in such case, apparently, corresponds to the following scheme:

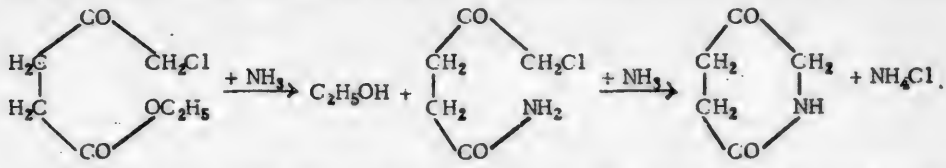
1) In the solution, upon neutralization at room temperature the salt is formed



2) During evaporation, there occurs ring closure of the salt solution



A similar course of reaction has also been observed in other cases. Thus, while attempting to obtain the δ-chlorolevulinic acid amide from chloroanhydride and ethyl ether, there was isolated quantitatively ammonium chloride and a highly hygroscopic oil, crystallizing with difficulty over P_2O_5 and again melting rapidly in air. It can be assumed that in this case as well, there proceed reactions with formation of a six-membered ring, namely:



The second stage, with formation of ammonium chloride crystals in the reaction mixture, proceeds during distillation of the alcohol. The oil resulting in this case, containing nitrogen, was not investigated because of its extreme hygroscopicity and small amount, and attempts to convert it to the semicarbazone and picrate were unsuccessful.

EXPERIMENTAL

1. Condensation of γ-chloroacetoacetic ester by means of sodium ethylate. 15 g of γ-chloroacetoacetic ester (b.p. 107-108° at 15 mm) was introduced into a flask equipped with condenser and calcium chloride tube, and a sodium alcoholate solution, prepared from 2.1 g of metallic sodium and 60 ml of absolute ethyl alcohol, was introduced through a dropping funnel in small amounts with hand stirring. Heat evolution from the mixture took place, with separation of a white, fluffy precipitate, with a simultaneous change in color of the reaction mixture from colorless to pink and then to red-brown.

Reaction mixture temperature was maintained for an hour at a temperature not exceeding 40°, for which purpose cooling with ice water from time to time was carried out, and the mixture then heated on a water bath, not exceeding 60°, to disappearance of the alkaline reaction. After termination of heating, there separated from the reaction mixture cooled to room temperature, a precipitate which was filtered off. Sodium chloride was extracted from the precipitate and 4.5 g of colorless crystals, consisting of succinylsuccinate ester resulted, m.p. of which was 127° after washing with absolute alcohol. Yield was 38.6% of theory.

Found %: C 56.01, 56.14; H 6.39, 6.19. M 264.2, 253.5. $C_{12}H_{16}O_6$. Calculated %: C 56.25; H 6.25. M 256.25.

2. Interaction of potassium phthalimide with γ-chloroacetoacetic ester. 50 ml of xylene was introduced into a flask equipped with reflux condenser and calcium chloride tube, followed by 6 g of potassium phthalimide in small portions and 5 g of γ-chloroacetoacetic ester of b.p. 104-107° at 14 mm.

Reaction was carried out for about a half-hour at room temperature, and then the reaction mixture was heated on a water bath at 60°. Since the flask contents resinified noticeably upon heating, the mixture, therefore, was left at room temperature for the night. On the following day, the precipitate (8.6 g) was filtered off from the reaction mixture, the former consisting of potassium chloride, phthalimide (m.p. 231°) and potassium phthalimide. Xylene was distilled off from the filtrate with steam, and there resulted a residue of 2.2 g succinylsuccinate ester, with m.p. 127°. A sample mixed with ester prepared in a preceding experiment did not give depression in melting point.

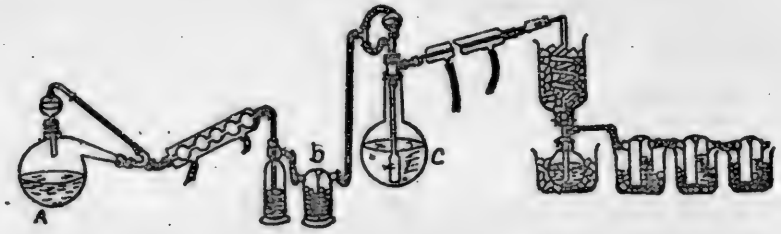
The yield of succinylsuccinate ester was 56.4% of theory.

Found %: C 55.98, 55.99; H 6.10, 5.75. $C_{12}H_{16}O_6$. Calculated %: C 56.25; H 6.25.

3. Synthesis of δ-chlorolevulinic acid ethyl ester. a) Preparation of an ethereal solution of diazomethane. To synthesize an ether solution of diazomethane on a standard work bench (without draft), using nitrogen obtained from ammonium chloride and sodium nitrite, a fine apparatus for efficient trapping of toxic gas was assembled (see Figure). Nitrogen received from retort A, is dried in receiver B. Reaction is carried out in flask, C, at such a rate that the diazomethane forming can be absorbed completely in the first three absorption flasks.

b) Synthesis of 4-diazo-3-butanoncarboxylic acid ethyl ester. 700-800 ml of filtered diazomethane ether solution containing about 8 g of gas, was introduced into a flask equipped with calcium chloride tube. The solution was precooled to −5° and then was introduced carefully, in small quantities, into 15 g of succinic acid chloroanhydride ethyl ester, b.p. 102-105° at 17 mm.

During addition of the chloroanhydride, there was observed an energetic evolution of nitrogen, and formation of a white, flaky precipitate. Reaction proceeded for about an hour, and then ceased completely.



The reaction mixture was left for the night at room temperature, the flask being sealed with a calcium chloride tube. On the following day the reaction mixture, containing a small residue of diazomethane, was filtered and the ether distilled out until ¼ of the original volume was reached. The residue containing ethyl ester of 4-diazo-3-butanoncarboxylic acid was decomposed with dry hydrogen chloride.

c) Synthesis of the ethyl ester of δ-chlorolevulinic acid. The resulting ester solution of 4-diazo-3-butanoncarboxylic acid was decomposed with dry hydrogen chloride at a temperature of −5 to −10°. At the start of saturation, very violent evolution of nitrogen proceeded, after which the nitrogen evolution proceeded more mildly. Saturation was complete after 4-5 hours. After termination of the saturation, solvent was partially distilled out of the reaction mixture in order to remove excess hydrogen chloride. 150-200 ml of fresh ester was added to the residue, the solution washed twice with water, then with 5% soda solution, and then with water to a neutral reaction of the wash waters. The wash waters were also extracted with ether, the ether solution washed to a neutral reaction, and this extract added to the main ether solution. The ether solution was dried over calcium chloride. After distilling off the solvent, 15.6 g (96.3% of theory) of crude product resulted – the ethyl ester of δ-chlorolevulinic acid, in the form of a dark-red oil, which was purified by double distillation in a flask with dephlegmator. B.p. was 115-120° at 10 mm (137-140° at 20 mm, 230-235° at 760 mm). Yield of pure ester was 14.63 g (90% of theory).

The resulting ester was an oil with faint odor, corrosive action on the skin, and especially upon the mucous membrane of the eye. It was readily soluble in alcohol, ether, chloroform, and was insoluble in water.

Found %: Cl 19.88, 19.94. $C_7H_{11}O_3Cl$. Calculated %: Cl 19.86.

4. Synthesis of δ-chlorolevulinic acid. 5 g of the ethyl ester of δ-chlorolevulinic acid and 50 ml of hydrochloric acid solution (1: 3) were placed in a flask equipped with reflux condenser and the mixture heated on a water bath to complete dissolution of the oil. The resulting solution was evaporated on a water bath almost to dryness. 25 ml of distilled water was added, and evaporation again carried out. Treatment of the dry residue with water, for complete removal of hydrogen chloride, was repeated until vapors of hydrochloric acid were hardly noticeable. Upon cooling the evaporated solution, 4 g of unpurified δ-chlorolevulinic acid resulted, which melted at 67-68°. The yield of crude acid was almost quantitative.

After two recrystallizations from benzene, 3.7 g of δ-chlorolevulinic acid resulted: crystalline platelets, 72-73.5°. Yield of purified acid was 88%.

Found %: C 40.10, 40.04; H 4.79, 4.64; Cl 23.91, 23.90; g-equiv. 149.2, 150.4. $C_5H_7O_3Cl$. Calculated %: C 39.87; H 4.69; Cl 23.57; g-equiv. 150.46.

5. Synthesis of the semicarbazone of δ-chlorolevulinic acid. According to Zelinsky [9], a mixture was prepared from 6.7 g of semicarbazide hydrochloride, 5.6 g of sodium acetoacetate and 20 ml of water. 1 g of the δ-chlorolevulinic acid was dissolved in 5 ml of water and mixed with 5 ml of the prepared mixture (double amount with respect to theory being taken). Needle crystals of the semicarbazone precipitated very rapidly. After three recrystallizations from methyl alcohol, m.p. was 148-149° (with decomposition). The yield amounted to 80% of theory.

Found %: N 20.31, 20.62. $C_6H_{10}O_3N_3Cl$. Calculated %: N 20.25.

SUMMARY

1. It has been established that γ-chloroacetoacetic ester reacts with sodium ethylate forming the succinylsuccinate ester.

2. It has been found that when attempt is made to condense γ-chloroacetoacetic ester with potassium phthalimide, there is also formed the succinylsuccinate ester, and not the δ-phthaliminoacetoacetate.

3. A satisfactory method for synthesis of δ-chlorolevulinic acid and ester has been developed, not described hitherto in the literature.

4. The impossibility of separating (under usual conditions) the salts and the amide of δ-chlorolevulinic acid has been demonstrated.

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CHARACTERIZATION OF β-(α-NAPHTHYL)-β-ALANINE

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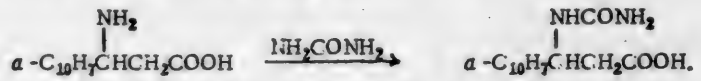
β-(α-Naphthyl)-β-aminopropionic acid, certain of its acyl derivatives, and their amides have been described earlier [1].

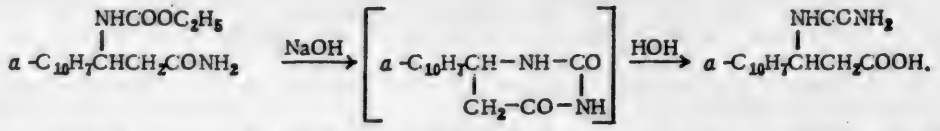
Synthesis of β-(α-naphthyl)-β-alanine differs somewhat from the usual method, and was carried out by heating α-naphthaldehyde in a solution of glacial acetic acid with slight excess of malonic acid (25%) and a large excess of ammonium acetate (125-250%). Naphthylaminopropionic acid separates readily from the resulting by-product, α-naphthylacrylic acid, either in the hydrochloride form [1], or by careful treatment of a mixture of the two compounds with ethyl ether, which dissolves only the naphthylacrylic acid.

A modification was introduced [2] in the method of preparing initial α-naphthaldehyde, resulting from heating of α-chloromethylnaphthalene with hexamethylenetetramine, which consists of replacing water-alcohol medium with 50% acetic acid solution. The yield of α-naphthaldehyde was accordingly increased from 30 to 75%.

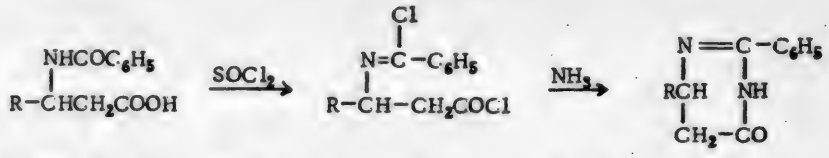
β-(α-Naphthyl)-β-aminopropionic acid gives many reactions characteristic for the β-amino acids. Thus, when heated with urea, it forms readily the corresponding β-ureido acid:



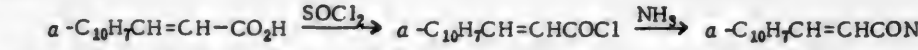
The same compound is formed when the amide is heated with alkali, according to the reaction proposed by Zvorykina and Rodionov [3]:



More complex is the course of reaction for formation of 2-phenyl-4-alkyl(aryl)-6-oxotetrahydropyrimidines [4]. The method for deriving these compounds consists in the interaction of N-benzoylated β-amino acids with thionyl chloride, and subsequent treatment with ammonia:

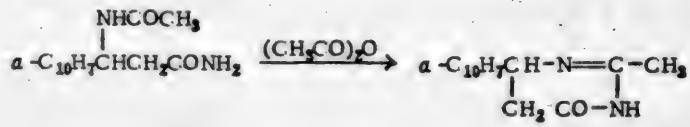


It was found that during the normal course of reaction with N-benzoylnaphthylalanine, there occurred chiefly a large amount of resinification and desamination; it was possible to isolate only a small quantity of naphthylacrylic acid amide.



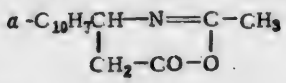
The corresponding 2-phenyl-4-naphthyl-6-oxotetrahydropyrimidine resulted in small yield only when the N-benzoylnaphthylalanine was treated with thionyl chloride in benzene solution, with subsequent amination, or upon heating the amide of the benzoylated alanine derivative with benzoyl chloride or acetic anhydride.

2-Methyl-4-naphthyl-6-oxotetrahydropyrimidine formed very smoothly by reaction of N-acetylnaphthylalanine with acetic anhydride:



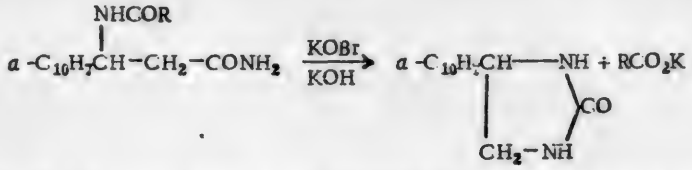
Conversion of naphthyl-β-alanine to 4-α-naphthylglyoxalidone was realized in two ways.

1) Interacting amides of acylated alanines with alkaline hypobromites according to the Hofmann reaction. The N-acyl derivatives, and their amides required for this purpose, were prepared by the method described earlier. It should be mentioned here that when heating naphthylalanine with acetic anhydride under the conditions in question [1], there was established the formation of a by-product (m.p. 234°), apparently an oxazine derivative:

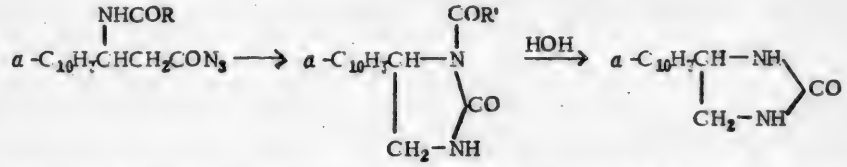


Investigation of this compound is still underway.

Interaction of acylated amides with hypobromite proceeds, as a rule, with simultaneous rupture of the acyl group:

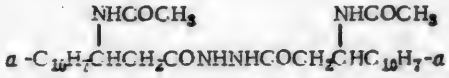


2) Heating N-acylated azides in dry benzene according to the Curtius reaction. Good yield results of readily hydrolyzable N-acylated α-naphthylglyoxalidone:



Esters, hydrazides and azides for this purpose were prepared according to a method developed earlier by the authors for other β-alanine derivatives [5].

In the synthesis of azide, resulting from N-acetylnaphthylalanine hydrazide reaction with sodium nitrite in acetate solution, there was established, along with the main product, formation of 1,2-di-[N-acetyl-β(α-naphthyl)-β-alanyl] hydrazine:



EXPERIMENTAL

β-(α-Naphthyl)-β-alanine. 16 g of α-naphthaldehyde, 13.4 g of malonic acid, 32 g of ammonium acetate and 40 g of glacial acetic acid were heated on a boiling water bath for 7 hours. After cooling, the solidified mass was washed twice with cold water (in 130 ml portions), to remove ammonium acetate and acetic acid. The water extract was brought to a weakly alkaline reaction with soda. Upon standing, 4 g of amino acid precipitated with m.p. 214-215°.

The residue, after treatment with water, represented a mixture of β-amino acid and α-naphthylacrylic acid, which can be separated by either of two methods.

1) Dilute hydrochloric acid is poured over the mixture and allowed to stand for 2-3 hours, after which it is filtered off from unsaturated acid, the precipitate washed with dilute hydrochloric acid and water. The acid filtrate and wash waters are combined, extracted with ether, and the acid aqueous solution evaporated to dryness. The amino acid hydrochloride results.

2) The residue is separated by prolonged treatment (over 120 hours) with ether in a Soxhlet apparatus. β-Amino acid does not dissolve in ether and can be filtered off. The total yield of β-amino acid was 13.5-16.6 g, i.e., about 60-74% of theory. Yield of the unsaturated acid was 20-26%.

β-(α-Naphthyl)-β-ureidopropionic acid. 0.2 g of β-(α-naphthyl)-β-alanine, 0.6 g of urea, and 4 ml of water 1.5 ml of 1 N-hydrochloric acid and 2-3 drops of alcohol were heated for several hours on a boiling water bath. After completion of the reaction, the liquid was filtered off, extracted twice with ether and acidified with strong

hydrochloric acid. The transparent liquid was rapidly poured off from the resin which formed and rolled up into a ball, from which, after 10-15 minutes, there precipitated out large crystals of the ureido acid. The melting point was not sharp; the substance melted at 105-110°, evidently in its own water of crystallization, solidified, and then melted again at 163-165°. The yield was 0.18-0.19 g (about 68%). After recrystallization from alcohol, the m.p. was 170-171°. The substance crystallized with 2 molecules of water.

Found %: Water of crystallization 12.25. $C_{14}H_{14}O_3N_2 \cdot 2H_2O$. Calculated %: H_2O 12.24.

The same compound was obtained by heating β-(α-naphthyl)-β-(N-carboethoxy)alanine with a weak alkaline solution. 0.15 g of urethane amide was heated with 7.5 ml of 5% sodium hydroxide to complete solution, filtered from slight turbidity, and the filtrate acidified with hydrochloric acid. After prolonged standing, a coarse crystalline precipitate (0.09 g) separated, which melted, first at 105-110°, and then at 163-165°. The preparation, recrystallized from alcohol, melted at 170-171°, and did not give depression of melting point in mixed sample with the above-described compound.

Naphthylcarboethoxyalanine was prepared by standard procedure. 2 g of β-(α-naphthyl)-β-alanine was dissolved in 25 ml of 2% sodium hydroxide solution, cooled with ice water, and 1.5 g of chlorocarbonic ester introduced with vigorous stirring. The reaction liquid was stirred for another 40 minutes and acidified with hydrochloric acid to a Congo red reaction. The separated precipitate was filtered off and dried. Yield was 1.85 g. M.p. 168-173°. For analysis, the carboethoxy compound was dissolved in aqueous alcohol and shaken several times with ether. The water-alcoholic solution was concentrated in vacuo. Upon cooling, a pure substance separated in the form of small needles with m.p. 175-177°.

Found %: N 5.20. $C_{15}H_{17}O_4N$. Calculated %: N 4.87.

N-Acetyl-β-(α-naphthyl)-β-alanine. 10 g of β-(α-naphthyl)-β-alanine was dissolved in 75 ml of approximately 10% potassium hydroxide, and 8.3 g of acetic anhydride added, gradually, with mixing. After standing 30 minutes, it was acidified with dilute hydrochloric acid (1:1). The oily precipitate which separated crystallized rapidly. The crystals were pressed out and washed with water. Yield was 11.6 g (about 97%). Melting point of the crude substance was 187-193°. After recrystallization from water, hexagonal prisms precipitated, melting at 193-194.5°.

Found %: N 5.21, 5.15. $C_{15}H_{15}O_3N$. Calculated %: N 5.45.

After acetylating 6 g of naphthylalanine by 15 minute boiling with 15 g of acetic anhydride, followed by removal of the latter by distillation in vacuo, there resulted about 7 g of a yellowish substance with m.p. 182.5-193°. Upon its recrystallization from water, 4.8 g (about 72%) of the acetyl derivative resulted with m.p. 193-194.5°, identical with the above-described, and about 0.8 g of a substance insoluble in water, with m.p. 234°. Recrystallization from glacial acetic acid did not increase the melting point. A sample mixed with the acetyl derivative produced lowering of the melting point to 185°. The substance was soluble in 1% alkali, giving a gelatinous precipitate with concentrated alkalies.

Found %: N 6.01, 5.91. Oxazine derivative $C_{15}H_{13}O_2N$. Calculated %: N 5.86.

N-Acylated naphthylalanine amides. Obtained through standard procedure by heating with thionyl chloride at 40° almost to cessation of hydrogen chloride evolution. After removal of excess $SOCl_2$ in vacuo, the residue was dissolved in dry benzene and treated by passing in dry ammonia. The separated amide was filtered off, washed with ether, 2-3% alkali hydroxide, and finally water.

β-(α-Naphthyl)-β-(N-carboethoxy)-alanine amide. The yield of purified amide from 1.5 g of the urethane, after recrystallization from alcohol, amounted to 1.0 g (66.7%).

Found %: N 9.82. $C_{16}H_{18}O_3N_2$. Calculated %: N 9.79.

β-(α-Naphthyl)-β-(N-acetyl)-alanine amide. 1.78 g of amide with m.p. 237-243° resulted from 2.5 g of β-(α-naphthyl)-β-(N-acetyl)-alanine. After recrystallization from alcohol, it precipitated in the form of long, angular needles, melting at 254-255°. The yield of purified substance was 1.5 g (about 60%).

Found %: C 70.44, 70.63; H 6.35, 6.48; N 11.17, 11.12. $C_{15}H_{16}O_2N_2$. Calculated %: C 70.27; H 6.30; N 10.94.

β-(α-Naphthyl)-β-(N-benzoyl)-alanine amide. 1.75 g (87.5%) of amide with m.p. 258-260° resulted from 2 g of β-(α-naphthyl)-β-(N-benzoyl)-alanine. The product, recrystallized from pyridine or dioxane, melted at 276.5-277°. It crystallized from dioxane in the form of needle clusters.

Found %: C 75.96, 76.09; H 5.92, 5.73; N 8.98, 8.92. $C_{20}H_{18}O_2N_2$. Calculated %: C 75.43; H 5.70; N 8.80.

2-Phenyl-4-(α-naphthyl)-6-oxotetrahydropyrimidine. Tetrahydropyrimidines are formed by heating N-benzoylated phenyl- or alkyl-alanines with thionyl chloride at 80°, with subsequent dry ammonia treatment. On carrying out this reaction with naphthyl alanine, resinification occurred and only naphthylacrylic acid amide was isolated. It was possible to obtain the corresponding 2-phenyl-4-naphthyl-6-oxotetrahydropyrimidine in low yield only under milder conditions.

For this purpose, 4.2 g of N-benzoyl-α-phthylalanine, 6 g of thionyl chloride and 10 g of dry benzene were heated with gentle boiling for about 4 hours, after which the benzene and thionyl chloride excess were distilled off in vacuo. The remaining brown viscous mass was extracted with ether. With external ice cooling, the ether solution was saturated with dry ammonia and filtered off from the precipitate which separated. The latter was washed with ether and hot chloroform. The insoluble residue was washed with water and recrystallized from alcohol. There resulted about 0.7 g of N-benzoylnaphthylalanine amide with m.p. 277°, which did not give depression in melting point with pure known amide. During evaporation of the ether-chloroform solution in air, a precipitate resulted with m.p. 177-180°. After recrystallization from chloroform, the melting point increased to 187-188° and remained constant. Yield was 0.5-0.6 g (about 13%).

2-Phenyl-4-(α-naphthyl)-6-oxotetrahydropyrimidine crystallized in the form of slightly yellow platelets, readily soluble in hot chloroform, alcohol and benzene.

Found %: N 9.23, 9.22. $C_{20}H_{16}ON_2$. Calculated %: N 9.33.

A very low yield of tetrahydropyrimidine derivative resulted upon heating of the N-benzoyl-naphthylalanine amide with benzoyl chloride and acetic anhydride. The reacylation reaction was not established in the latter case.

Upon heating the N-acetyl-derivative with acetic anhydride, the yield of 2-methyl-4-naphthyloxotetrahydropyrimidine amounted to 80% of theory. Silky needles (from ether). M.p. 148-149°.

Found %: N 11.32, 11.57. $C_{15}H_{14}ON_2$. Calculated %: N 11.76.

Interaction of N-benzoyl-β-(α-naphthyl)-β-alanine amide and hypobromite. 2 g of amide was introduced into a solution of hypobromite, prepared from 20 ml of 15% sodium hydroxide solution and 2.4 g of bromine at −7°, and the mixture stirred at room temperature. After 2 hours, the precipitate slowly became oily, and after another 75 minutes, a yellow viscous mass formed. Stirring was terminated and the reaction mass heated to 78-80° for 20 minutes, whereupon the resinous mass melted and then solidified again. After cooling, the precipitate was filtered off and washed with water. 0.95 g of the substance with m.p. 195-203° was isolated. After recrystallization from alcohol, there resulted 0.22 g with m.p. 221.5-222°. From the analysis and properties, this compound corresponded to naphthylglyoxalidone In mixed samples with 3-N-benzoyl-4-(α-naphthyl)-glyoxalidone, obtained according to the Curtius reaction, there was depression of melting point, but there was no depression in melting point when mixed with 4-(α-naphthyl)-glyoxalidone, obtained by saponification of acylglyoxalidone (see below).

Found %: C 73.74, 73.97; H 6.19, 6.00; N 13.41, 13.24, 13.11. $C_{13}H_{12}ON_2$. Calculated %: C 73.54; H 5.71; N 13.21.

Upon acidification of the alkaline solution, and subsequent extraction by ether, there resulted 0.77 g of the substance. The latter was distilled with steam. About 0.5 g of benzoic acid was isolated from the distillate. From its melting point and from other properties, the undistilled residue was found to be N-benzoyl-β-(α-naphthyl)-β-alanine.

At times it was possible to isolate a small amount of benzoylnaphthylglyoxalidone during the Hofmann reaction with N-benzoylnaphthylglyoxalidone amide. The difficulties in separating the acyl derivatives from the non-acylated substance is explainable by the similarity of all of the reactions and the close melting points, for preparation of the benzoylated and acetylated naphthyloxalidone of which the Curtius reaction is more applicable (see below).

Interaction of N-Acetyl-β-(α-naphthyl)-β-alanine amide and hypobromite. 2.34 g of amide was introduced into a hypobromite solution prepared from 20 ml of 15% NaOH solution and 3 g of bromine at −12°, and the mixture stirred at room temperature. After 30 minutes the amide was completely dissolved. The solution was heated. At 50° a light, white precipitate separated; at 55-60° a brown oil separated, which crystallized upon further heating. The mixture was kept for several minutes at 80°. After cooling, the precipitate was filtered off, washed with water. 1.25 g of substance with m.p. 208-215° resulted; after recrystallization from alcohol, 0.71 g with m.p. 217-220°. The resulting compound gave depression of melting point for a mixed sample with 2-N-acetyl-4-(α-naphthyl)-glyoxalidone, prepared according to the Curtius reaction, but did not give depression in mixed sample with the above-described naphthylglyoxalidone

Hofmann reaction with β-(α-naphthyl)-β-(N-carboethoxy)-alanine amide. 0.15 ml of bromine and 0.3 g of amide were added to 5 ml of 15% sodium hydroxide solution. After standing 2-3 hours (with periodic stirring) all of the amide went into solution, and a thick oil precipitated to the bottom of the flask. The reaction mass was heated to 60° and then cooled. The solid substance which precipitated out after separation from the liquid and drying, weighed 0.17 g and melted at 203-205°. After recrystallization from alcohol, the melting point rose to 221°. The product did not give depression with known pure naphthylglyoxalidone.

Ethyl ester of N-benzoyl-β-(α-naphthyl)-β-alanine. Hydrogen chloride was passed for 4 hours through a solution of 10 g of N-benzoylamino acid and 50 ml of absolute alcohol at 60-70°, and the reaction mixture then cooled to 0°, the solution saturated with hydrogen chloride and left overnight. The solvent was removed in vacuo and the residue washed with water and extracted with ether. The ether extract was washed with a weak solution of sodium bicarbonate and water, and dried over anhydrous sodium sulfate. After removal of the ether, there remained a rapidly solidifying oil. After recrystallization from alcohol, and washing with a small volume of ether, the m.p. was 109-110° (the melting point remained unchanged with a second recrystallization). Needle clusters precipitated from alcohol. Yield was 9.72 g (89.3%).

Found %: N 3.84, 3.76. $C_{22}H_{21}O_3N$. Calculated %: N 4.03.

About 0.3 g of initial N-benzoylamino acid was isolated from the wash solutions upon acidification.

Ethyl ester of N-acetyl-β-(α-naphthyl)-β-alanine. Product was obtained under the ethylating conditions of the N-benzoyl derivative. The ethyl ester of the N-aceto derivative was less soluble in ether after removal of the solvent in vacuo, and upon addition of water and ether, a copious crystalline precipitate separated. The precipitate and the ether solution were washed with a weak solution of sodium bicarbonate, and then with water.

The yield from 7.2 g of N-acetylamino acid ester was 7.3 g, or 91% of theory. M.p. was 136-139° after recrystallization from alcohol, and washing with a small volume of ether raised it to 142.5-143°. Elongated, tetraangular platelets precipitated from alcohol.

Found %: N 5.16, 4.99. $C_{17}H_{15}O_3N$. Calculated %: N 4.91.

N-benzoyl-β-(α-naphthyl)-β-alanine hydrazide. A mixture of 9.7 g of the ethyl ester of N-benzoylamino acid, 4.1 ml of hydrazine hydrate and 11 ml of absolute alcohol was heated to moderate boiling. After 15-20 minutes, a thick crystalline mass formed, to which was added 2 ml of absolute alcohol and the heating continued for another 1.5-2 hours on a water bath. After cooling, the precipitate was filtered off and washed on a filter with water, alcohol and ether. Yield was 9 g (96.6%). M.p. 254-256°, remaining unchanged by recrystallization. Elongated tetrangular platelets precipitated from the alcohol.

Found %: N 12.76, 12.69. $C_{20}H_{19}O_2N_3$. Calculated %: N 12.61.

N-Acetyl-β-(α-naphthyl)-β-alanine hydrazide. This was obtained under the conditions of N-benzoyl hydrazide derivative formtation. The yield was about 5.7 g, or 92.2% of theory, from 6.5 g of the ethyl ester of N-acetylamino acid. M.p. was 236-237°, and did not change after recrystallization from water.

Found %: N 15.49, 15.54. $C_{15}H_{17}O_2N_3$. Calculated %: N 15.5.

N-Benzoyl-β-(α-naphthyl)-β-alanine azide. 5 g of the hydrazide of N-benzoylamino acid was dissolved in 235 ml of 87-88% acetic acid, the solution cooled to 0°, and 3.6 g of finely-powdered sodium nitrite introduced in 3 to 4 portions over 15 minutes with shaking. After 5 minutes, the azide precipitated in the form of fine needles. The reaction mixture was left for 1.5 hours at 0°, and was then diluted with ice water. The azide precipitate was filtered off, washed with ice water to the disappearance of acetic acid odor, and dried in a desiccator. The yield was about 4.7 g (91%). M.p. was 83-84.5° (with decomposition).

N-Acetyl-β-(α-naphthyl)-β-alanine azide. 0.24 g of hydrazide was treated with 2.5 ml of 82% acetic acid. The mixture was cooled to 0-2°, and, with shaking, 0.31 g of finely-powdered sodium nitrite was introduced, whereupon the hydrazide dissolved completely. After 2 hours at 0°, the reaction solution was diluted with ice water. An oily product separated from the emulsion formed, which soon crystallized in the form of quadrangular prisms. The precipitate was filtered off, washed with ice water to disappearance of acetic acid odor and dried in a desiccator. Yield of azide was about 0.21 g (83%). M.p. 74-75° (with decomposition).

On carrying out the reaction in an acetate solution a substance of higher molecular weight was formed along with the azide in a series of experiments, which was separated from the azide by dissolution of the latter, with heat, in benzene. Thus, from 2.64 g of hydrazide, 0.43 g of substance with m.p. 265-270° resulted, insoluble in both acid and alkaline media. Upon heating to boiling in 2-3% sodium hydroxide solution, the melting point increased to

287-292°. The compound isolated was apparently the 1,2-di(N-acetyl-β-alanyl)hydrazine. An identical product resulted on heating the hydrazide in glacial acetic acid.

Found %: C 70.30, 70.44; H 5.97, 6.06; N 10.84, 10.92. $C_{30}H_{30}O_4N_6$. Calculated %: C 70.55; H 5.92; N 10.98.

4-(α-Naphthyl)-3-N-benzoylglyoxalidone. A solution of 4.7 g of azide in 250 ml of dry benzene was heated to boiling for 5 hours. The benzene was almost completely distilled off. After cooling, the precipitate formed was filtered off. After drying, 3.85 g of substance with m.p. 210-218° resulted. After recrystallization from alcohol, 3.05 g (about 70.7%). M.p. 222-224°, unchanged after second recrystallization. Elongated tetrangular platelets precipitated from alcohol.

Found %: N 8.57, 8.66. $C_{20}H_{16}O_2N_2$. Calculated %: N 8.86.

3-N-Acetyl-4-(α-naphthyl)-glyoxalidone. A solution of 1.75 g of N-acetyl-β-(α-naphthyl)-β-alanine azide in 75 ml of dry benzene was heated to boiling for 4 hours. After removal of benzene, 1.56 g (about 99%) of yellowish powder was left with m.p. 220-225°. After recrystallization from alcohol and benzene, m.p. 214-216°. Hexagonal prisms from alcohol precipitated.

Found %: C 71.10, 71.28; H 5.74, 5.84; N 10.66, 10.86. $C_{15}H_{16}O_2N_2$. Calculated %: C 70.83; H 5.55; N 11.02.

Saponification of 3-N-Benzoyl-4-(α-naphthyl)-glyoxalidone. 1 g of N-benzoyl-glyoxalidone was heated to moderate boiling in 50 ml of 15% NaOH solution for 5 hours. No visible changes occurred. After cooling the residue was filtered off, and washed with water. 0.74 g of substance with m.p. 185-205° resulted. Elongated tetragonal platelets precipitated from alcohol upon recrystallization, m.p. 219.5-221.5°. The yield was 0.24 g. In addition, through partial evaporation of the mother liquor, there was obtained another 0.12 g of substance with m.p. 215-219°; thus the total yield constituted 53.6% of theory. Mixed samples of the compound derived from the initial benzoyl derivative gave a depression in melting point, which did not occur when it was mixed with 4-(α-naphthyl)-glyoxalidone, obtained according to the Hofmann method. At the same time benzoic acid in about 78% of theory was isolated.

Saponification of 3-N-acetyl-4-(α-naphthyl)-glyoxalidone. 0.5 g of 3-N-acetyl-4-(α-naphthyl)-glyoxalidone was heated to gentle boiling in 25 ml of 15% sodium hydroxide solution for 5 hours. After cooling, the precipitate was filtered off and washed with water. 0.4 g of substance resulted (95.8% of theory), with m.p. 220-222°. After recrystallization from alcohol, elongated tetragonal platelets precipitated. M.p. was 221-222°. A mixed sample of the product with initial N-acetylnaphthylglyoxalidone gave a depression in melting point, which did not occur when mixed with 4-(α-naphthyl)-glyoxalidone.

SUMMARY

1. Synthesis of β-(α-naphthyl)-β-ureidopropionic acid has been carried out by two procedures: heating of β-(α-naphthyl)-β-alanine with urea, and heating of N-carboethoxynaphthylalanine with dilute alkali.

2. It has been determined that in the usual synthesis of 2-phenyl-4-aryl(alkyl)-6-oxotetrahydropyrimidine (heating of N-benzoylated-β-alkyl (aryl)-β-alanines with thionyl chloride and subsequent treatment with dry ammonia), N-benzoyl-β-(α-naphthyl)-β-alanine does not give ring closure, and upon desamination, forms α-naphthylacrylic acid amide.

3. It has been found that desired phenylnaphthylpyrimidine can be obtained in low yield by treating N-benzoylnaphthylalanine with thionyl chloride under milder conditions (heating in benzene medium). The same compound can be obtained by interacting N-benzoylnaphthylalanine with benzoyl chloride or acetic anhydride.

4. Conversion of β-(α-naphthyl)-β-alanine to naphthylglyoxalidone has been accomplished by both the Hofmann reaction (interacting the amides of acylated naphthylalanines with alkaline hypobromite) and according to the Curtius reaction (boiling the acylated naphthylalanine azides in benzene solution). In the latter case, acylated α-naphthylglyoxalidones are formed in high yield.

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HOFMANN REACTION WITH α-BROMOSUBSTITUTED ACID AMIDES

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In 1905 N. M. Kizhner [1] for the first time used the Hofmann reaction on α-bromosubstituted acid amides for the synthesis of cyclobutanone from α-bromocyclobutancarboxylic acid, and made the assumption that this reaction course with amides of the aliphatic α-bromosubstituted acid should lead to formation of aldehyde or ketone, depending upon structure of the acid.

He confirmed this assumption by synthesizing acetone from α-bromosubstituted acid amide. In 1908 [2] Mossler made an observation that when α-bromosubstituted acid amides are heated with alkali, rupture of HCN proceeds, with formation of aldehydes; however, Mossler did not isolate the aldehydes and did not carry out their quantitative determination, but instead, made his deductions on the basis of qualitative reactions and quantitative determination of HCN. In 1934 Brown [3] obtained aldehydes from α-bromosubstituted acid amides, utilizing the Curtius reaction.

In the present work the Hofmann reaction was carried out with α-bromoisovaleric, α-chlorocaproic, α-bromoenanthic, α-bromoundecyclic, α-bromodiethylacetic and α,α'-dibromoadipic acid amides. Reaction was carried out in both hypobromite solution and in sodium hypochlorite solution. The best yields of aldehydes resulted by treatment of α-bromosubstituted amides with alkaline hypochlorite solution, and immediate removal of the forming aldehyde from the sphere of reaction. Aldehyde yield depends upon its boiling point. The best yield (65-69% of theory) is obtained with the lowest boiling, isobutyric aldehyde; N-capric aldehyde resulted in 23% yield of theory.

To clarify the question of how the nature of the halogen affects the reaction course, experiments were set up with α-chlorocaproic acid amide. Replacement of bromine by chlorine did not increase aldehyde yield. All experiments with the monobasic acid amides, with exception of diethylacetic acid amide, were accompanied by considerable resin formation. The amount of resin increased with increase in boiling point of the resulting aldehyde. Reaction with α-bromodiethylacetic acid amide proceeded with extensive destruction of the molecule, and instead of diethylketone, the aldehyde was obtained. Diethylketone formed only in that case where reaction was carried out with large excess of alkali. α,α'-Dibromoadipic acid diamide under conditions of the Hofmann reaction, produced neither aldehyde nor resin. There was isolated from the reaction mixture succinic acid in the amount 10-11% of the amide taken.

In experiments arranged for the purpose of synthesizing urethanes both under normal conditions and in sealed tubes, the initial α-bromosubstituted amide resulted quantitatively in all cases.

EXPERIMENTAL

Hofmann Reaction with α-Bromoisovaleric Acid Amide

α-Bromoisovaleric acid was obtained in 80% yield according to the method proposed for α-bromocaproic acid [4]. On reaction with PCl_3, the acid was converted into chloroanhydride, which, with vigorous mechanical stirring, was then added slowly to 33% ammonia solution cooled to −5°.

4.5 g of amide (0.025 mole) with m.p. 132° was introduced in small portions with mechanical stirring into the hypobromite solution obtained at −5° from 4 g of NaOH (0.1 mole), 35 ml of water and 1.28 ml (0.025 mole) of bromine. The last portion of amide, while dissolving, caused decolorization of the solution. The slightly turbid, colorless solution was transferred to a flask for steam distillation, and was heated with a stream of steam as rapidly as possible. The solution immediately became turbid and foamy at 50-70°, the aldehyde distilling off rapidly with the steam. The ammonia which distilled off along with the aldehyde was duly neutralized with hydrochloric acid; 35 ml of 4% $NH_2OH \cdot HCl$ in 60% alcohol was added to the solution. After a half-hour the hydrochloride which separated was titrated with 0.6835 N KOH: vol. = 15.38 ml; aldehyde found − 0.757 g (42%).

Reaction with Sodium Hypochlorite

The hypochlorite was prepared by passing a current of chlorine at −5° into 8 g of NaOH (0.2 mole) in 70 ml of water until the weight increase reached 3.6 g (0.05 mole). 9 g (0.05 mole) of α-bromoisovaleric acid amide

was introduced into the resulting solution with mechanical stirring, after which the reaction mixture was distilled with steam. The receiver was immersed in cooling mixture. The resulting distillate was distilled a second time; the second distillate was salted out with sodium chloride. The aldehyde was separated, dried and distilled. 2.26 g (63%) resulted, b.p. 64-66°. Melting point of the 2,4-dinitrophenylhydrazone was 181.5°.

Reaction with α-Bromoenanthic Acid Amide

α-Bromoenanthic acid amide was prepared in the same manner as the α-bromoisovaleric acid amide. White crystals, readily soluble in a majority of organic solvents, insoluble in cold and poorly soluble in hot water. M.p. 58° (from ligroin).

Found %: N 6.84; Br 38.61. $C_7H_{14}ONBr$. Calculated %: N 6.73; Br 38.46.

5 g (0.025 mole) of α-bromoenanthic acid amide was added to the sodium hypochlorite solution prepared as in the preceding experiment. The cooled amide solution was added to the hypochlorite solution in the flask by a dropping funnel, the flask being set up for steam distillation, heated on a boiling water bath; superheated steam was passed through the flask. The aldehyde distilled off with steam was extracted with ether. After drying with sodium sulfate, and distilling off the ether, 1.4 g (56%) of caproic aldehyde with b.p. 128-131° resulted. Melting point of the 2,4-dinitrophenylhydrazone was 104°.
Found %: N 19.96, 19.89. $C_{12}H_{15}O_4N_4$. Calculated %: N 20.00.

Reaction with α-Bromoundecylic Acid Amide

α-Bromoundecylic acid amide was synthesized from undecylic acid by the same procedure as with the preceding amides, with 70% yield, calculating on the basis of chloroanhydride. White crystals, insoluble in both cold and hot water, soluble in hot methanol. M.p. 59° (after two recrystallizations from methanol).

Found %: N 5.76; Br 30.55, 30.31. $C_{11}H_{22}ONBr$. Calculated %: N 5.30; Br 30.30.

9.9 g of α-bromoundecylic acid amide (0.0375 mole) was dissolved in 50 ml of methanol and was added, with mechanical stirring, to the sodium hypochlorite solution obtained at −5° from 60 ml of water, 6 g (0.15 mole) of sodium hydroxide and 2.7 g (0.0375 mole) of chlorine. At first a thin suspension precipitated, which then dissolved rapidly, forming a transparent colorless solution. The cooled reaction mixture was added dropwise to the flask for steam distillation which was internally heated by a current of superheated steam, with simultaneous external heating. The distillate was extracted repeatedly with ether. After distilling off the ether, 1.8 g of the substance with b.p. 203-205° resulted. Melting point of 2,4-dinitrophenylhydrazone was 102°.

Reaction with α-Chlorocaproic Acid Amide

α-Chlorocaproic acid was obtained by chlorination of N-butylmalonic ester. 120 g (0.47 mole) of N-butylmalonic ester was placed in a three-necked flask equipped with stirrer, reflux condenser and bubbler for chlorine supply. The reaction mass was heated to 80° and a strong current of chlorine gas was passed through the liquid with vigorous stirring. Completion of reaction was determined by increased weight of absorbed chlorine. The calculated weight increase was 20 g, resulting weight increase was 22 g. 123 g of chlorobutylmalonic ester with b.p. 134-138° at 8 mm resulted.

To obtain the α-chlorocaproic acid, the ester was cooled to −10° and was mixed with 56 g of KOH in 500 ml of absolute alcohol solution precooled to −5°. After several minutes, the mixture solidified to a uniform white mass which was kept for 6 hours in a cooling mixture. The dipotassium salt of α-chloro-N-butylmalonic acid was filtered with suction, washed with small quantities of ether and dissolved in 200 ml of water. The solution was cooled to 0°, acidified with cooled dilute sulfuric acid to an acid reaction with Congo red, and extracted with ether. The ether extract was dried with sodium sulfate. After distilling off the ether, decarboxylation of N-butyl-α-chloromalonic acid was carried out by slow distillation in vacuo from a flask with dephlegmator. There resulted 33 g with b.p. 120-122° at 10 mm.

To synthesize α-chlorocaproic acid chloroanhydride, 21 g (0.15 mole) of phosphorus trichloride was added to the obtained preparation over a period of 2 hours at 80-85°, and the reaction mixture then kept for 4 hours at 100-105° to the cessation of HCl evolution. The α-chlorocaproic acid chloroanhydride was used without further purification for synthesis of the amide. The amide resulted in 61% yield of theory according to the above-described procedure. Lustrous white leaflets, m.p. 61° (from water).

Found %: N 9.41, 9.29; Cl 23.29, 23.35. $C_6H_{12}ONCl$. Calculated %: N 9.36; Cl 23.74.

The Hofmann reaction was carried out under the same conditions as for α-bromoenanthic acid amide. n-Valeric aldehyde resulted in 65.5% yield of theory. B.p. 100-102°. Melting point of the dinitrophenylhydrazone was 98°.

Reaction with α-Bromoundecylic Acid Amide

α-Bromoundecylic acid resulted in 57.5% yield of theory on reacting dry bromine with undecylic acid in the presence of 1 ml of phosphorus trichloride. B.p. 156-165° at 4 mm. The chloroanhydride was obtained by addition of PCl_3 at 85-90°, with subsequent holding at 110-115° for 4-5 hours. Yield was 64% of theory, b.p. 130-136° at 6 mm.

The amide was synthesized under the above-described conditions; yield 70%. White crystals insoluble in both cold and hot water, soluble in methanol. After two crystallizations from methanol, the m.p. was 59°.

Found %: N 5.76; Br 30.31, 30.55. $C_{11}H_{22}ONBr$. Calculated %: N 5.31; Br 30.30.

The amide was insoluble in hypochlorite, and therefore, to carry out the experiment it was first dissolved in methanol, and the resulting solution then added to hypochlorite. The Hofmann reaction was carried out under the same conditions as in the preceding experiments. For isolation of the aldehyde, the reaction mixture was added from a dropping funnel to the flask which was heated from within by superheated steam, and at the same time from without. Yield was 23% of theory. Melting point of the dinitrophenylhydrazone was 102°.

Reaction with α-Bromodiethylacetic Acid Amide

Reaction was carried out with α-bromodiethylacetic acid amide under the same conditions as for the other acids, and was accompanied by extensive decomposition of the substance. The distillate gave qualitative reactions for aldehyde.

7.35 g (0.038 mole) of α-bromodiethylacetic acid amide were dissolved in sodium hypochlorite prepared from 7.3 g (0.182 mole) of NaOH, 73 ml of water and 2.7 g (0.038 mole) of chlorine (4.8 mole alkali per 1 mole of amide and 1 mole of chlorine). Steam was passed through the resulting solution. The distillate was extracted with ether. 0.8 g (25%) of the substance with b.p. 101° resulted. Melting point of the dinitrophenylhydrazone of diethylketone was 155.5°.

Found %: N 21.26, 21.10. $C_{11}H_{14}O_4N_4$. Calculated %: N 21.05.

Reaction with α,α'-Dibromoadipic Acid Diamide

α,α'-Dibromoadipic acid diamide was obtained by reacting 25% ammonia solution with the diethyl ester of α,α'-dibromoadipic acid. Yield was 60-65%. The amide was insoluble in cold water, and hydrolyzed readily upon boiling with water; very poorly soluble in all organic solvents. Lustrous white needles. After recrystallization from benzene, m.p. was 183° with decomposition.

Found %: C 23.61, 23.65; H 3.28, 3.18; N 9.01, 8.99; Br 53.12, 52.81. $C_6H_{10}O_2N_2Br_2$. Calculated %: C 23.84; H 3.31; N 9.27; Br 52.98.

15 g (0.05 mole) of α,α'-dibromoadipic acid diamide was dissolved in hypochlorite prepared from 140 ml of water, 16 g of NaOH and 7.2 g of chlorine. The transparent, almost colorless, solution was added to the flask by means of a dropping funnel, through which flask a stream of superheated steam was passed. The flask for steam distillation was placed in a boiling water bath. During the entire distillation, the solution in the flask remained transparent, no resin forming. Qualitative test for aldehyde in the distillate was negative. The amount of ammonia in the distillate constituted 65% of theory. The solution left after steam distillation was evaporated to 150 ml, cooled to 0°, acidified with dilute H_2SO_4 to an acid reaction with Congo red. The separated bromine was tied up by addition of a small amount of concentrated $NaHSO_3$ solution. The solution was extracted with ether, the ether extract dried with sodium sulfate. After distilling off the ether, 0.6 g of crystalline substance remained, which was pressed out onto a porous plate, and washed with dry ether. M.p. 187-188°. The sample mixed with pure succinic acid did not give a depression in melting point.

SUMMARY

The Hofmann reaction has been carried out with amides of α-bromoisovaleric, α-chlorocaproic, α-bromoenanthic, α-bromoundecylic, α-bromodiethylacetic and α,α'-dibromoadipic acids.

The best yields of aldehydes result when α-bromosubstituted amides are treated with an alkaline solution of hypochlorite with immediate removal of the forming aldehyde from zone of reaction.

Replacement of bromine by chlorine does not increase aldehyde yields.

During reaction of α-bromodiethylacetic acid amide, aldehyde is formed instead of diethyl ketone. Diethylketone results in that case where reaction is carried out with large excess of alkali.

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SYNTHESIS OF 2-MERCAPTO-IMIDAZOLYL-PROPIONIC ACID

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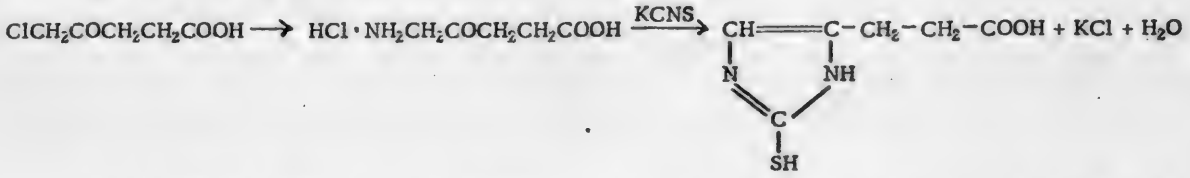
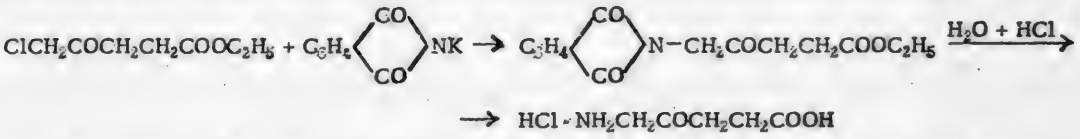
It follows from the literature that synthesis of many imidazole derivatives is a rather complex problem.

In studying various procedures for synthesis of these compounds, it was found that it is possible to obtain, in very good yields, 2-mercapto-imidazolyl-propionic acid, and related compounds, from δ-chlorolevulinic acid, according to the following scheme:



The first stage of this synthesis is the preparation of δ-aminolevulinic acid hydrochloride, according to the Gabriel method [1], from the ethyl ester of δ-chlorolevulinic acid and potassium phthalimide:



By hydrolyzing the ethyl ester of δ-phthalylaminolevulinic acid, as with the work of Rodionov and Yartseva [2], it was also possible to isolate an intermediate hydrolysis product – δ-phthalylaminolevulinic acid.

Condensation of the ethyl ester of δ-chlorolevulinic acid and potassium phthalimide was carried out in absolute alcohol, the reaction mixture being boiled on a water bath. The reaction products were found, on one hand, to be the ethyl ester of δ-phthalylaminolevulinic acid and potassium chloride, and on the other – phthalimide and a highly resinified viscous oil, whose composition and structure were not investigated.

After removal of potassium chloride from the hot reaction mixture by filtration, there precipitated from the filtrate upon cooling colorless, crystalline platelets of δ-phthalylaminolevulinic acid ethyl ester, with m.p. 81-82°. Yield was 51% of theory. Analytical data for nitrogen, carbon and hydrogen corresponded completely to those calculated according to the formula $C_{15}H_{15}O_5N$. The ethyl ester of δ-phthalylaminolevulinic acid is not described in the literature, and has been synthesized for the first time.

Upon hydrolysis of the resulting ester, two new compounds were isolated which have not been described in the literature: the hydrochloride of δ-aminolevulinic acid and δ-phthalylaminolevulinic acid.

The hydrochloride of δ-aminolevulinic acid resulted on boiling the ethyl ester of δ-aminolevulinic acid in a dilute solution of hydrochloric acid (1:1). The hydrochloride crystals separated from reaction solution after removal of the phthalic acid, and the filtrate, decolorized by charcoal, was evaporated to as small a volume as possible. Melting point of the pure hydrochloride was 150-151°. Yield was 93%. Analytical data for chlorine and nitrogen corresponded to that calculated according to the formula $C_5H_{10}O_3NCl$.

δ-Phthalylaminolevulinic acid was obtained by hydrolysis of the ethyl ester by heating to complete dissolution in a dilute solution of hydrochloric acid (1:3). A colorless, fluffy precipitate, composed of small crystalline needles, separated out from the reaction mixture upon cooling, with m.p. 159°. The yield was 85% of theory. Analytical data for nitrogen corresponded to the formula $C_{13}H_{11}O_5N$. In addition, 2-mercapto-imidazolyl-propionic acid, described for the first time by Akabori [4], was synthesized from δ-aminolevulinic acid hydrochloride and potassium thiocyanate according to the Wohl and Marckwald method [3]. 2-Mercapto-imidazolyl-propionic acid represented colorless, crystalline needles, soluble in water with heating, and readily soluble in alcohol and acetic acid; after repeated recrystallizations, the m.p. was 207-208°. Yield was 72.7% of theoretical amount.

Analytical data for nitrogen and for water of crystallization coincided well with the calculated, according to the formula $C_6H_8O_2N_2S \cdot H_2O$.

2-Mercapto-imidazolyl-propionic acid was obtained for the first time from the hydrochloride of aldehydo-glutamic acid and potassium thiocyanate in 40% yield; m.p. was 205-206.5°.

EXPERIMENTAL

Synthesis of the Ethyl Ester of δ-Phthalylaminolevulinic Acid

10 g of the ethyl ester of δ-chlorolevulinic acid in 60 ml of absolute ethyl alcohol and 10.1 g of potassium phthalimide were introduced into a flask equipped with reflux condenser and a calcium chloride tube. The mixture was heated on a water bath for 5 hours, moderate boiling being maintained in the flask.

By the end of the heating period, the nature of the precipitate was considerably changed externally: the light, fluffy precipitate changing into finely-crystalline. After termination of the heating, the resulting potassium chloride (3.6 g) which precipitated was filtered from the hot solution. After cooling, there precipitated from the filtrate colorless, crystalline platelets, in the form of elongated rectangles, consisting of δ-phthalylaminolevulinic acid ethyl ester (9.4 g). The ether was distilled off and purified by recrystallizing from benzene. The purified ester of δ-phthalylaminolevulinic acid melted at 81-82°. The yield was 8.25 g (51%). The side-products of the reaction were found to be phthalimide (2.5 g) and an oil (5.25 g) of unknown composition, which gave upon storage additional quantities of δ-phthalylaminolevulinic acid ethyl ester, phthalimide and potassium chloride. Saponification of the oil did not produce new products other than phthalic acid.

Found %: C 62.24, 62.48; H 5.17, 5.20; N 4.93, 5.08. $C_{15}H_{15}O_5N$. Calculated %: C 62.26; H 5.23; N 4.85.

Synthesis of δ-Phthalylaminolevulinic Acid

2.9 g of δ-phthalylaminolevulinic acid ethyl ester (m.p. 80-81°) and 25 ml of hydrochloric acid solution (1:3) were placed in a flask equipped with reflux condenser. The mixture was heated on a wire gauze for 20 minutes, whereupon the ester dissolved and the oil dissolved by saponification. Following this, heating was terminated. There was observed upon cooling copious separation of loose, light precipitate in the form of needle crystals.

δ-Phthalylaminolevulinic acid was readily soluble in alcohol, in water with heating, and poorly soluble in ether. After recrystallization from alcohol, the m.p. was 159°. Yield was 85% of theory.

Found %: N 5.62, 5.61. $C_{13}H_{11}O_5N$. Calculated %: N 5.37.

Semicarbazone of δ-Phthalylaminolevulinic Acid

0.52 g of δ-phthalylaminolevulinic acid was dissolved in 2 ml of alcohol diluted with 2 ml of water; 0.6 ml of the semicarbazide solution, prepared according to Zelinsky [5], was added to the resulting solution. Soon after pouring in the solution, crystals of δ-phthalylaminolevulinic acid semicarbazone precipitated out, insoluble in water, poorly soluble in alcohol. After recrystallization from alcohol, the m.p. was 202-203°, with decomposition, yield 97%.

Found %: N 17.73; 17.90. $C_{14}H_{14}O_5N_4$. Calculated %: N 17.61.

Synthesis of δ-Aminolevulinic Acid Hydrochloride

6 g of δ-phthalylaminolevulinic acid ethyl ester (m.p. 80-81°) and 90 ml of hydrochloric acid solution (1:1) were introduced into a flask equipped with reflux condenser and gas outlet tube terminating over water. The reaction mixture was heated on a wire gauze to gentle boiling for 6 hours, and then left overnight. On the following day 3.4 g of phthalic acid (m.p. 200-202°) was filtered off. The filtrate was evaporated to one-half volume, boiled with activated charcoal, and again evaporated to the point of crystalline film formation on the surface of the solution. Upon cooling of the filtrate, 2.45 g of colorless crystals separated, which melted at 150-151°. In addition, there was recovered from the mother liquor after evaporation, 0.8 g of the hydrochloride (m.p. 145-147°). The total yield of hydrochloride was 3.25 g (93%).

Found %: N 8.62, 8.65; Cl 21.19. $C_5H_{10}O_3NCl$. Calculated %: N 8.36; Cl 21.16.

Semicarbazone of δ-Aminolevulinic Acid Hydrochloride

1 g of the hydrochloride of δ-aminolevulinic acid was dissolved in 3 ml of 50% methyl alcohol, and to the

resulting solution was added 2 ml of the semicarbazide mixture, prepared according to Zelinsky [5]. Copious separation of crystals proceeded very rapidly. The semicarbazone obtained was poorly soluble in alcohol, readily so in water with heating. Yield was 1.2 g (90%). The semicarbazone, recrystallized from methyl alcohol, melted at 204.5° with decomposition.

Found %: N 25.28; Cl 15.91, 15.96. $C_6H_{13}O_3N_4Cl$. Calculated %: N 24.95; Cl 15.79.

Synthesis of 2-Mercapto-imidazolyl-propionic Acid

4 g of δ-aminolevulinic acid hydrochloride was dissolved in 50 ml of water, and 5 g of potassium thiocyanate in 10 ml of water; the solutions were mixed and left overnight at room temperature.

On the following day, the reaction mixture was evaporated on a water bath until a crystalline film appeared on the surface of the solution, whereupon it was then cooled and the colorless crystals of 2-mercapto-imidazolyl-propionic acid which precipitated then filtered off. The resulting acid was liberated by separation of potassium chloride from its solution in hot absolute alcohol (35-45 ml). The mineral salt was filtered off, and solvent distilled off from the filtrate, and the resulting crystalline residue again dissolved in water (25 ml) with heating. There resulted from the solution 3.3 g of colorless, needle-like crystals of 2-mercapto-imidazolyl-propionic acid monohydrate. In addition, another 0.5 g of the same acid was isolated from the mother liquor. The crystals of 2-mercapto-imidazolyl-propionic acid (3.8 g) were once again dissolved in water (7.5 ml) with heat, and upon cooling, colorless crystals, with m.p. 202-204°, were isolated. The yield was 3.3 g (72.7%). After repeated recrystallizations from water, there resulted the acid with a m.p. of 207-208°.

Found %: N 14.27; water of crystallization 9.30, 9.37. $C_6H_8O_2N_2S \cdot H_2O$. Calculated %: N 14.74; water of crystallization 9.47.

SUMMARY

1. Optimal conditions for synthesis of δ-aminolevulinic acid hydrochloride, not described in the literature, have been developed.

2. A new method for synthesis of 2-mercapto-imidazolyl-propionic acid, in almost double the yield as compared with the literature data, has been found.

3. δ-Phthalylaminolevulinic acid ethyl ester, δ-phthalylaminolevulinic acid, and the semicarbazones of δ-aminolevulinic acid hydrochloride and δ-phthalylaminolevulinic acid have been prepared in good yields.

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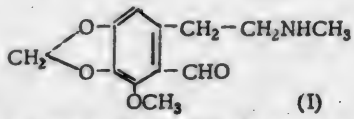
THE CHARACTERIZATION OF COTARNINE, HYDRASTININE, THEIR BENZOYL DERIVATIVES, AND INTERACTION OF COTARNONE WITH MALONIC ACID AND AMMONIA

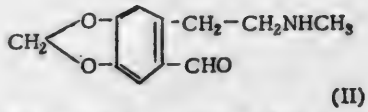
V. M. Rodionov and M. G. Chentsova

It has been demonstrated many times that cotarnine (I) and hydrastinine (II) can react in three tautomeric forms, one of which is found to be the aldehyde form.



(I)

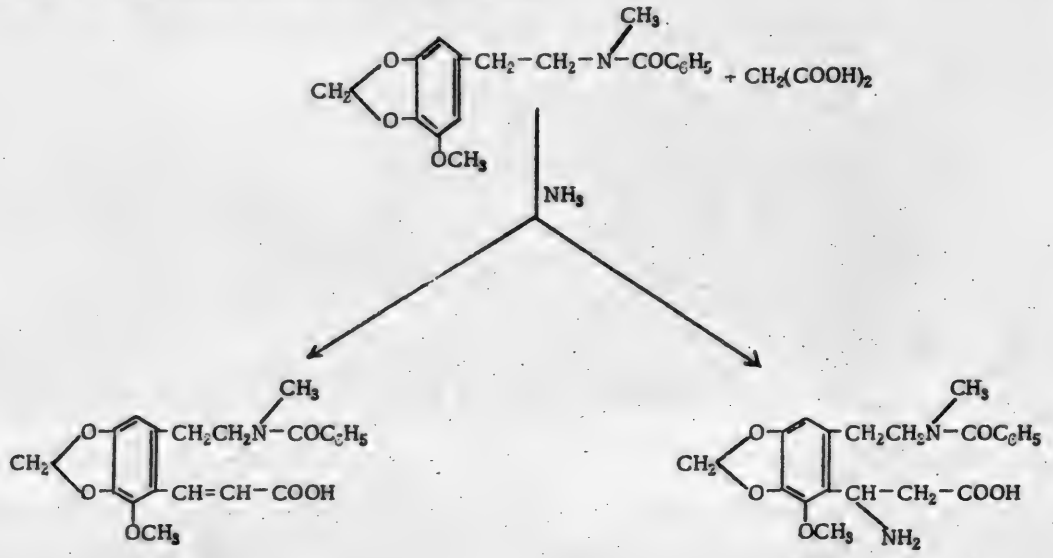
and



(II)

The presence of an aldehyde group is confirmed by the many characteristic reactions of these compounds, for example, of dismutation [1], of condensation with substances containing active hydrogen such as acetone, nitromethane, malonic ester [2], and so forth.

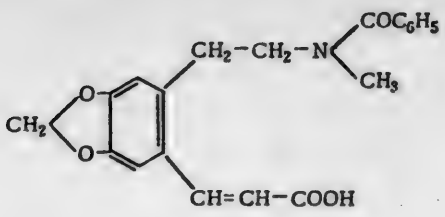
The feasibility of such a structure for cotarnine and for hydrastinine prompted an investigation of their condensation reactions with malonic acid in the presence of ammonia, according to the method of Rodionov [3], in order to obtain new complex β-amino acids. The reaction was carried out with cotarnine and its derivatives, benzoylcotarnine and cotarnone, as well as with benzoylhydrastinine. It was found, under normal conditions of synthesis, that the main reaction product is an unsaturated acid; the yield of β-amino acid was relatively small. Upon condensing with benzoylcotarnine, an unsaturated acid (III) resulted in 68% yield, calculated for benzoylcotarnine, and the β-amino acid (IV) in 15-15.5% yield.



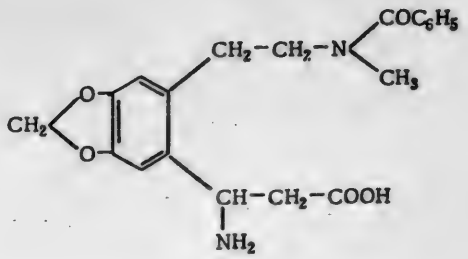
(III) (IV)

To characterize the β-amino acid (IV), its benzoyl and p-nitrobenzoyl derivatives were prepared. The unsaturated acid (III) was converted into the ester, and its dibromo- and monobromo- derivatives were obtained as well. This acid was apparently synthesized at an earlier date by Ahlers, but was not isolated in chemically pure form [4].

Under the same conditions of condensation, benzoylhydrastinine gave about 6% of an unsaturated acid (V) and 22% of β-amino acid (VI):



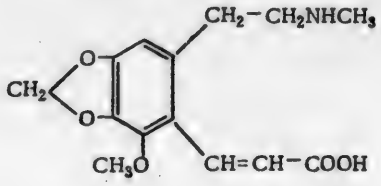
(V)



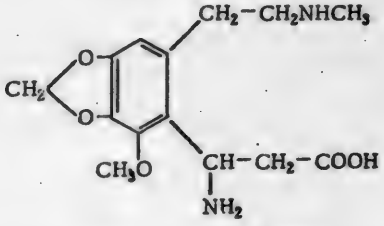
(VI)

The unsaturated character of the acid (V) was confirmed by its conversion into the dibromo derivative.

Reaction of malonic acid and ammonia with cotarnine resulted in a mixture of two amino acids (VII) and (VIII), difficult to separate, from which it was possible to isolate only the unsaturated amino acid (VII) in chemically pure form:



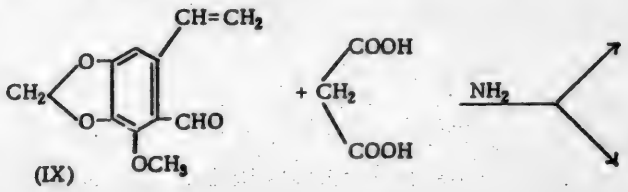
(VII)



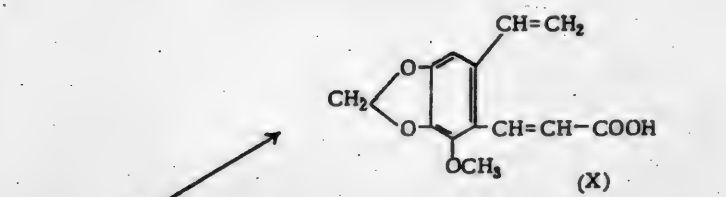
(VIII)

The acetyl derivative of the unsaturated acid (VII) was obtained earlier by Bouman [2], by condensation of cotarnine with acetic anhydride; the unsaturated acid, its ethyl ester, as well as the dibromo derivative, are described by E. A. Postovskaya.

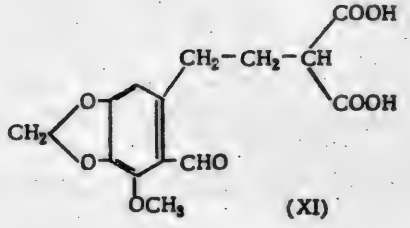
During synthesis of the cotarnine derivative, cotarnone (IX), there were isolated two unsaturated acids—a monobasic (X) and apparently a dibasic (XI); no amino acid was found.



(IX)



(X)



(XI)

For determination of the unsaturated acid structure (X), it was converted into the tetrabromo derivative.

EXPERIMENTAL

Condensation of Benzoylcotarnine With Malonic Acid and Ammonia

30 g of benzoylcotarnine, 50 g of 11% ammonia solution in absolute ether and 10 g of malonic acid were heated on a water bath in a flask with upright condenser for 3.5-4 hours. The bath temperature was slowly raised in order to distill off the alcohol and ammonia gradually, and the bath was heated to boiling only during the last hour. After termination of the heating, the residue in the flask, representing a brown, vitreous mass, was dissolved in a small excess of 5% soda solution, which was separated from suspended impurities by filtration, and precipitated by hydrochloric acid. A precipitate of the unsaturated acid (III) formed, a viscous, light-yellow, poorly crystallizing mass. Weight of the air-dried product was 23 g (about 68%).

The acid was readily soluble in alcohol and acetic acid, poorly so in benzene, chloroform, and very poorly in water. It decolorized bromine water and permanganate solution. After three recrystallizations from 50% acetic acid, m.p. was 132-133°.

Found %: N 3.79; g-equiv. 377.1, 381.7. $C_{21}H_{21}O_8N$. Calculated %: N 3.65; g-equiv. 383.2.

The solution separated from the precipitate of unsaturated acid, containing the hydrochloride of β-amino acid (IV), as well as excess malonic acid and a small amount of unsaturated acid, was evaporated to dryness on a water bath. The dry residue was dissolved in absolute alcohol to separate mineral salts, and again evaporated to dryness, followed by solution in a small volume of water to remove traces of unsaturated acid, and after another evaporation, was dissolved in as small an amount of absolute alcohol as possible.

The β-amino acid hydrochloride was then isolated by precipitation with absolute ether in the form of a viscous mass, converting into white crystals upon repeated washings with ether in the porcelain funnel.

After drying over phosphorus pentoxide, it melted at 115° (with decomposition). The yield was 6 g, 15.6% relative to benzoylcotarnine. A highly hygroscopic substance, very soluble in water and alcohol.

Found %: N 6.72; Cl 8.51, 8.23. $C_{21}H_{25}O_7N_2Cl$. Calculated %: N 6.41; Cl 8.13.

Isolation of β-Amino Acid (IV) From the Hydrochloride

A solution of sodium hydroxide was added to an aqueous solution of 4 g of silver nitrate to the point of complete precipitation. The precipitate was washed repeatedly by decantation, and then mixed with a solution of 1.3 g of the above-described β-amino acid hydrochloride (IV). The mixture was warmed slightly and left overnight. The solution, containing the silver salt of the amino acid, was filtered off from the precipitate, and the silver precipitated with hydrogen sulfide. The liquid which was filtered off, was evaporated and after dissolving in a small volume of absolute alcohol, the β-amino acid was precipitated out with absolute ether. The acid was very soluble in water and alcohol. Fine, colorless crystals, not melting. Yield was 0.85 g (71.0%).

Found %: N 6.94. $C_{21}H_{24}O_5N_2$. Calculated %: N 7.00.

Benzoylation of β-Amino Acid (IV)

4.5 g of the β-amino acid hydrochloride (IV) was dissolved in 54 g of 10% NaOH solution and heated to 40-45°. At this temperature, and with vigorous stirring, 8 g of benzoyl chloride was added dropwise over 1-1.5 hours, and the mixture then heated for another 2 hours. The β-amino acid benzoyl derivative which separated in the form of a heavy, oily liquid, was isolated from the reaction mixture and recrystallized from benzene. M.p. was 213-214°. Yield was 3.1 g (61%).

Found %: N 5.78, 5.86; g-equiv. 492, 496. $C_{28}H_{28}O_7N_2$. Calculated %: N 5.55; g-equiv. 504.2.

Synthesis of the p-Nitrobenzoyl Derivative of β-Amino Acid (IV)

The p-nitrobenzoyl derivative was prepared in 70-75% yield by the same method. After recrystallization from alcohol-ether mixture, the m.p. was 212-214°.

Found %: N 7.96. $C_{28}H_{27}O_9N_3$. Calculated %: N 7.65.

Bromination of the Unsaturated Acid (III)

Bromine solution in acetic acid was added dropwise to a solution of 10 g of unsaturated acid (III) in 30 ml of glacial acetic acid until bromine decolorization ceased. Reaction was carried out with ice cooling. After standing for 42 hours, the mixture was poured into 500 ml of water, whereupon the dibromo derivative of the unsaturated acid (II) immediately precipitated out as a solid. After crystallization from benzene, ether or acetic acid, the

m.p. was 181-183° (with decomposition). It was not possible to determine the equivalent weight of this acid by titration with alcoholic sodium hydroxide since HBr splits off.

Found %: Br 28.98, 28.99. $C_{21}H_{21}O_6NBr_2$. Calculated %: Br 29.48.

HBr Split Fromthe Dibromoderivative of the Unsaturated Acid (III)

A solution of 1 g of 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-6-methoxy-β-phenyl-α,β-dibromopropionic acid in 5 ml of ethyl alcohol was placed in a flask equippped with reflux condenser and heated with 0.3 g of NaOH solution in 2 ml of water on a water bath at 90° for 1 hour. Upon cooling, a copious precipitate of 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-6-methoxymonobromocinnamic acid sodium salt separated in the amount of 0.5 g. A solution of the salt slowly decolorized bromine water and potassium permanganate.

Found %: Br 15.56, 15.60. $C_{21}H_{19}O_6NBrNa$. Calculated %: Br 16.56.

Synthesis of Unsaturated Acid (III) Ethyl Ester

An aqueous solution of silver nitrate was added to a solution of 6 g of the unsaturated acid (III) in ethyl alcohol. The resulting precipitate of silver salt was filtered off, washed several times with water and alcohol, and dried over calcium chloride in a desiccator protected from light. The dry residue of silver salt was mixed with 10 g of ethyl bromide and 20 g of absolute alcohol in a flask equipped with reflux condenser, and was heated on a water bath to boiling for 2 hours. A heavy precipitate of silver bromide resulted. The precipitate was filtered off and the excess ethyl bromide plus some of the alcohol were distilled off from the filtrate. After cooling, the residue formed a thick mush of crystals of the ethyl ester of the unsaturated acid (III). The crystals were pressed out on a porous plate, dried, and then washed with a small volume of ether. M.p. was 106-109°. Yield was 4.2 g (65%).

To purify from unsaturated acid, the residue was dissolved in ether and the ether layer washed with 15% soda. After partial removal of solvent, the ester separated in the form of colorless, flaky crystals, with m.p. 109-110°.

Found %: N 3.72, 3.89. $C_{23}H_{25}O_6N$. Calculated %: N 3.40.

Condensation of Benzoylhydrastinine with Malonic Acid

Condensation and isolation of the reaction products were carried out in the same manner as with the above-described method for benzoylcotamine. From 4.8 g of benzoylhydrastinine, there were obtained 3.2 g (60%) of unsaturated acid (V) and 1.2 g (22%) of β-amino acid hydrochloride (VI).

The unsaturated acid, recrystallized from alcohol, melted at 177°; it decolorized bromine water and potassium permanganate solution.

Found: g-equiv. 357.6, 354.2. $C_{20}H_{19}O_5N$. Calculated: g-equiv. 353.

β-Amino acid hydrochloride melted at 140° (with decomposition).

Found %: N 7.19, 7.14. $C_{20}H_{23}O_5N_2Cl$. Calculated %: N 6.89.

Bromination was carried out under the same conditions as with bromination of the unsaturated acid (III).

The dibromo derivative, 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-β-phenyl-α,β-dibromopropionic acid, separated in the form of a viscous mass, crystallizing upon standing for several days. It crystallized from benzene or acetic acid. M.p. was 158-160° (with decomposition). It dissolved readily in alcohol and ether, very poorly in water.

Attempt to titrate with an alcoholic sodium hydroxide solution did not yield an equivalent point since it split off HBr.

Found %: Br 30.59, 30.55. $C_{20}H_{19}O_5NBr_2$. Calculated %: Br 31.16.

Condensation of Cotarnine with Malonic Acid and Ammonia

10 g of cotamine and 40 ml of a 12% alcoholic solution of ammonia in a flask equipped with upright condenser was left in a cooling mixture for a half-hour, and 4.5 g of malonic acid then poured in, and the temperature of the bath raised in such a manner that the alcohol distilled off over 3-3.5 hours. The mass remaining in the flask was dissolved in 15 ml of water by heating on a water bath and filtered. Upon cooling, a crystalline precipitate of the unsaturated 2-β-(N-methyl)-aminoethyl-4,5-methylendihydroxy-6-methoxycinnamic unsaturated amino acid (VII) resulted in the amount of 7.2 g (61%). After two recrystallizations from alcohol, and drying in a drying cabinet at

125°, the m.p. was 204-206°. It crystallized with 2 molecules of water. Melting point of the aqueous acid was 121-122°.

Found %: N 4.83, 4.65. $C_{14}H_{18}O_5N$. Calculated %: N 5.00.

The filtrate, after evaporation on a water bath, resinified, but the amino acid was not obtained in the pure state.

Condensation of Cotarnone with Malonic Acid and Ammonia

28 g of cotarnone, 9 ml of 11% alcoholic ammonia solution and 1.6 g of malonic acid were heated on a water bath in a flask equipped with vertical condenser, for 3.5-4 hours. The bath temperature was gradually raised in order that the alcohol and ammonia excess might distill off gradually, and only during the last hour was the bath heated to boiling. The resulting dry residue was repeatedly treated with benzene preheated to 30° and the benzene solution evaporated to 10-12 ml volume, thereupon, the crystals of unsaturated acid (X) separated. The acid dissolved in alcohol, benzene, acetic acid and ether, and decolorized bromine water and potassium permanganate solution. It crystallized out from alcohol or benzene with a m.p. of 177-179°. The analytical data and the gram equivalent value indicated that the substance was 2-vinyl-4,5-methylendihydroxy-6-methoxycinnamic acid. The yield was 1 g (29.7%).

Found %: C 62.81, 62.73; H 5.00, 5.05; g-equiv. 244.1. $C_{13}H_{12}O_5$. Calculated %: C 62.90; H 4.84; g-equiv. 248.

The residue, after isolation of the unsaturated acid (X) was dissolved in 40-50 ml of 5% soda solution, filtered to remove a small resinous precipitate, and was acidified with 10% hydrochloric acid solution to a strongly acid reaction. Thereupon, the dibasic acid separated, apparently being the γ-(2-aldehydo-3-methoxy-4,5-methylendihydroxy)-phenylpropandicarboxylic acid (XI). M.p. was 98° (with decomposition). The yield was 2.2 g (52%).

Found: g-equiv. 162.9. M 325.8. $C_{14}H_{14}O_8$. Calculated: M 310.

The total yield of unsaturated acids was 52.6 + 29.7 = 82.3%. After isolation of the dicarboxylic acid, the solution was evaporated in vacuo. The residue, upon evaporation, resinified, and the β-amino acid was not found.

Bromination of 2-Vinyl-4,5-methylendihydroxy-6-methoxycinnamic Acid

0.7 g of unsaturated acid (X) and 10 ml of dry carbon tetrachloride were placed in a flask equipped with reflux condenser and dropping funnel. The flask was cooled with a mixture of water and ice, and 3 ml of 10% bromine solution in carbon tetrachloride was then gradually added. All of the acid gradually went into solution. During the reaction no gas evolution was observed. The mixture was left overnight at room temperature.

A precipitate, consisting of the tetrabromoderivative of the acid taken, was formed. White crystals with m.p. 150° (from alcohol). The substance was poorly soluble in alkali. Yield was 1.6 g (99.9%).

Found %: C 27.33, 27.49; H 2.24, 2.15. $C_{13}H_{12}O_5Br_4$. Calculated %: C 27.46; H 2.11.

SUMMARY

It has been established that condensation, under the usual Rodionov synthesis conditions, of cotarnine and its derivative, benzoylcotarnine, and of cotarnone, as well as of benzoylhydrastinine, with malonic acid and ammonia, proceeds mainly in the direction of unsaturated acid formation: yield of amino acids is relatively poor.

New compounds which have been synthesized are:

1) the unsaturated 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-6-methoxycinnamic acid (III), its mono- and dibromo- derivatives and the ethyl ester;

2) the amino acid, 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-β-phenyl-β-alanine, (IV), its hydrochloride, benzoyl and p-nitrobenzoyl derivatives;

3) the unsaturated 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxycinnamic acid (V) and its bromo derivative;

4) 2-β-(N-methyl-N-benzoyl)-aminoethyl-4,5-methylendihydroxy-β-phenyl-β-alanine hydrochloride (VI);

5) 2-vinyl-4,5-methylendihydroxy-6-methoxycinnamic acid (X), the unsaturated acid (VII), and the tetrabromo derivative.

All of the ennumerated compounds have been synthesized and described for the first time.

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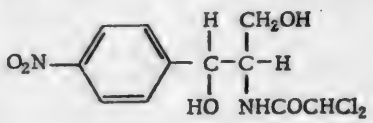
* See Consultants Bureau Translation, page 353.

RESEARCH IN THE CHEMISTRY OF CHLOROMYCETIN (LEVOMYCETIN)

II. A STUDY OF SYNTHETIC METHODS AND OF THE SYNTHESIS OF OPTICALLY-ACTIVE ANALOGS OF CHLOROMYCETIN (LAEVOMYCETIN) [1]

M. M. Shemyakin, E. M. Bambas, E. I. Vinogradova, M. G. Karapetyan, M. N. Kolosov, A. S. Khokhlov, Yu. B. Shvetsov and L. A. Shchukina

During the past few years, D-threo-1-(p-nitrophenyl)-2-dichloroacetylamino-1,3-propandiol (I) (chloromycetin, chloroamphenicol, laevomycetin) has attracted considerable interest, and has been investigated in detail, both in the medico-biological sense [2] and in the chemical sense [3].



(I)

One of the most intense lines of development of such investigations is a study of the relationship between structure and antibacterial activity in the chloromycetin series. At present methods of synthesis, and the synthesis of a considerable number (several hundred) of analogs and derivatives of this compound have been realized, many of which compounds have been tested biologically [3]. However, this type of research suffers one serious handicap of major proportion The crux of the matter lies in the fact that of the four stereoisomers of 1-(p-nitrophenyl)-2-dichloroacetylamino-1,3-propandiol, only one, namely, the D-threo-isomer (chloromycetin) possesses antibacterial activity. Therefore, a study of the relationship between structure and antibacterial activity for this series of compounds can give comparable results only in the event that the analogs tested possess the same steric configuration as chloromycetin. However, a study of this problem reveals that in a majority of cases compounds have been biologically tested whose steric structure remains obscure, resulting data on which, therefore, cannot be considered to be sufficiently convincing. Furthermore, there are no descriptions for general methods of synthesizing a series of the more important chloromycetin analog types with strictly-defined steric configuration. The only exception is that of the N- and O-acylchloromycetin analogs which can be obtained by acylation of D-threo-1-(p-nitrophenyl)-2-amino-1,3-propandiol, or its steroisomers under conditions which exclude the possibility of inversion or racemization. In the remaining cases, however, the steric structures of synthesized analogs has usually been judged only upon circumstantial evidence. To illustrate, if a given synthetic procedure* leads mainly to formation of D,L-threo-1-(p-nitrophenyl-)-2-dichloroacetylamino-1,3-propandiol (chloromycetin racemate), and not to its diastereoisomer, it has then been considered that all analogs likewise synthesized by this procedure would also possess the threo configuration. Such conclusions are of course not entirely convincing, particularly in view of the fact that even a small change in synthetic conditions can lead not to formation of the chloromycetin racemate, but instead to its biologically-inactive diastereoisomer** (for details see [3]).

Relative to that which has been stated above, the authors have attempted to develop general synthetic procedures for certain types of chloromycetin analogs which possess strictly-defined steric configuration, in order to obtain correlative data for solution of the problem of relation between structure and antibacterial activity for the series of compounds in question. At the same time we carried out another objective – to elucidate the steric structures of certain chloromycetin analogs obtained earlier by methodsalready described in the literature.

There are described below two synthetic methods developed by the authors for obtaining optically-active analogs of D-threo-1-(p-nitrophenyl)-2-dichloroacetylamino-1,3-propandiol (chloromycetin), differing from this compound by the presence of other substituents in the p-position of the benzene ring, in place of the nitro group.

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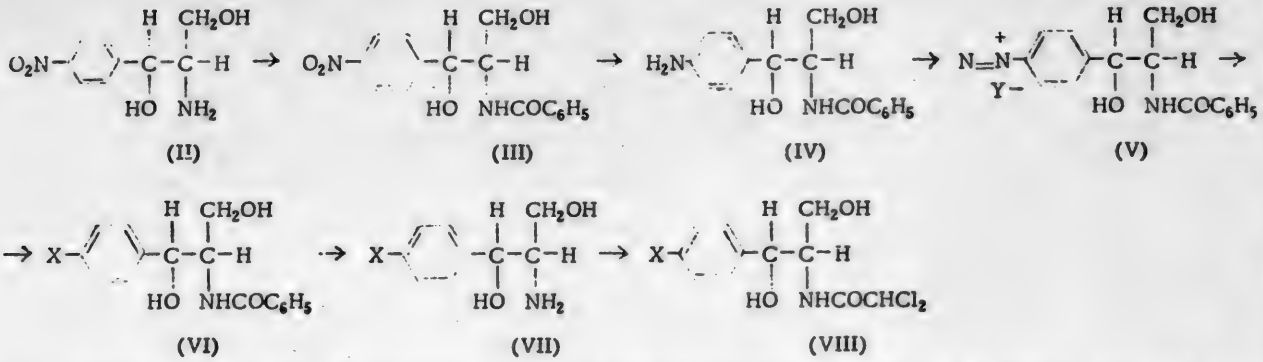
* For example, the Long and Troutman synthesis which has found extensive application, starts with p-substituted acetophenones [4].

** When for example synthesis is carried out, starting with p-nitrobenzaldehyde and glycine ester [5].

The two methods make it possible to proceed further with a compound of known steric configuration, and which does not change during the procedure of synthesizing the indicated analogs.

The first method is presented in Scheme 1.

Scheme 1



(II) (III) (IV) (V)

(VI) (VII) (VIII)

According to this chart, the synthesis of optically-active chloromycetin analogs of the general type (VIII) is realized by starting with the readily-accessible D- or L-threo-1-(p-nitrophenyl)-2-amino-1,3-propandiol (II).*

The first stage of synthesis —benzoylation of aminodiols (II) to give the corresponding N-benzoyl derivatives (III)— should be carried out by using the earlier-described procedure [6]. Yields reach 70-75%.

The second stage of synthesis —conversion of N-benzoyl nitro derivatives (III) to the amino compounds (IV)— can be effected by hydrogenation at 70-80° and 50 atmospheres in the presence of a nickel catalyst base; yield was 90-95% of theory. The reduction process can be carried out at room temperature and normal pressure, but in such case reaction proceeds a great deal slower.

The third stage of synthesis —diazotization of the amino compounds (IV)— is carried out in mineral acid solutions at 0-5°; however, this process proceeds very slowly (3-4 hours). The conditions of diazotization have to be modified somewhat, depending upon the type of radical which is to replace the diazo group. It should be mentioned that diazonium salts of the type (V), are quite stable in aqueous solutions, especially at low temperatures.

The fourth stage of synthesis —replacement of the diazo group in diazonium salts of the type (V) by various atoms or radicals (H, Cl, I, OH, CN, NO_2, AsO_3H_2)— can, in a number of cases, be carried out according to standard procedures, but at times (with replacement by I, OH, CN) it is necessary to maintain specific conditions.** Compounds of the general type (VI) which result from this reaction are often obtained satisfactorily (from 50 to 80% in the case of diazo group replacement by H, Cl, I and CN); however, with OH replacement the yield drops to 40%, and upon replacement with AsO_3H_2, to 20%. Diazo compounds of the type (V) readily undergo azo coupling, for example with β-naphthol, the corresponding azo dye resulting in 85% yield.

The fifth stage of synthesis —rupture of the N-benzoyl group in compounds of the general type (VI)— can, in a number of cases, be carried out by heating for several hours with 20% HCl. From chloro- and iodo-substituted compounds (VI), where X = Cl or I, there are formed the corresponding aminodiols, of general type (VII) in about 55% yield. With nitriles (VI: X = CN), rupture of the benzoyl group is accompanied by hydrolysis of the nitrile group to the carboxyl group, which results in compounds found to be the internal salt (yield 65%).

$$\bar{O}OC \cdot C_6H_4CHOHCH(\overset{+}{N}H_3)CH_2OH.$$

However, in the case of hydroxy compounds (VI: X = OH), 15 minutes heating with 1% HCl sufficies to rupture the benzoyl group; even under these conditions, however, hydrolysis is accompanied by such molecular changes that isolation of the individual compounds is difficult.

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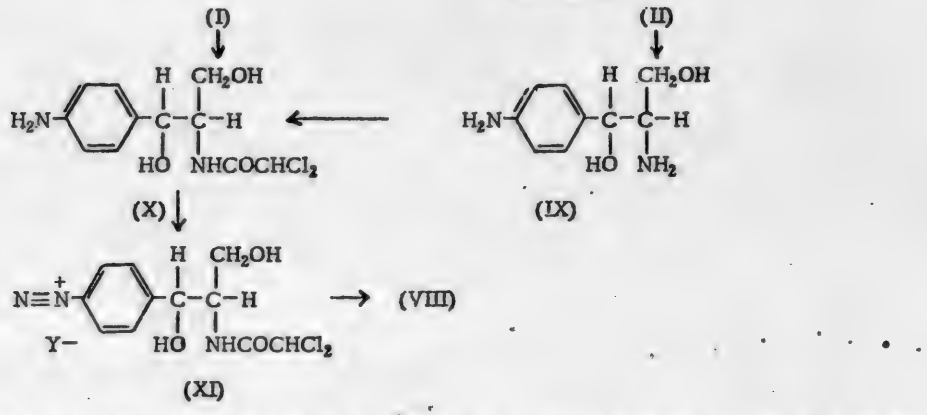
* For the sake of brevity, there are given in Schemes 1 and 2 formulas for the D-threo- series of compounds only.

** Thus, the replacement of diazo group by iodine proceeds satisfactorily only in the presence of KI in highly diluted solution, wherein the reaction should first be carried out at 0° and then at 20°. In synthesizing hydroxy compounds, it is necessary that initial pH value for the diazo solution be in the range 5-6, and the process itself carried out at 70-90°. On the other hand, replacement of the diazo group by the nitrile group proceeds satisfactorily in the presence of cuprous cyanide only when the initial pH for the medium is about 7 and the temperature about —5°.

The last (sixth) stage of synthesis – N-dichloroacetylation of aminodiols of the type (VII) to produce the optically-active chloromycetin analogs, of general type (VIII) – was achieved by two procedures, depending upon the character of the substituent situated in the para-position of the benzene ring. In the case of chloro- and of iodo-substituted aminodiols (VII: X = Cl or I), this reaction was carried out by heating them for a short period of time with the methyl ester of dichloroacetic acid at 90-95° (yield from 50-70%). However, in the case of carboxy-substituted aminodiols (VII: X = COOH) which are not capable of reacting with $Cl_2CHCOOCH_3$, even at 130°, the dichloroacetylation was then carried out by means of an ether solution of the dichloroacetic acid chloroanhydride in the presence of an aqueous solution of K_2CO_3 (yield about 70%).

Since the synthesis of chloromycetin analogs according to Scheme I is carried out via a large number of intermediate stages, and since some compounds of the type (VIII) (for example containing the cyano group) cannot be synthesized at all by this method, the authors developed a second procedure for synthesis of chloromycetin analogs of the type (VIII), as presented in Scheme 2.

Scheme 2



The great advantage of this chart of synthesis, as compared with the preceding, is the absence of hydrolytic stages and of dichloroacetylation, for here, in contrast to Scheme 1 the diazotization reaction and replacement of the diazo group by various atoms and radicals is carried out on N-dichloroacetyl derivatives of (X) type, which is found to be a quite accessible compound, which is not so for the N-benzoyl derivatives of type (IV).

At first, N-dichloroacetylation of the type compound (X) was carried out, proceeding from D- and L-threo-1-(p-nitrophenyl)-2-amino-1,3-propandiols (II) which were catalytically reduced to the corresponding diamines of the type (IX), with 90% yield, under conditions of (III) and (IV) hydrogenation. However, selective dichloroacetylation of diamines (IX) could be carried out only with the aliphatic amino groups, reacting them with the methyl ester of dichloroacetic acid at room temperature for 24 hours, with subsequent isolation of D- and L-threo-1-(p-aminophenyl)-2-dichloroacetyl-amino-1,3-propandiols (X) in their hydrochloride form (yields up to 25%). It was found later, however, to be more convenient to synthesize a compound of type (X) by reduction of D- and L-threo-1-(p-nitrophenyl)-2-dichloroacetylamino-1,3-propandiols (I) in the presence of a nickel catalyst base, at normal pressure and room temperature. It was established that if hydrogenation is terminated after absorption of one-half the theoretical hydrogen volume, then rupture of chlorine from the dichloroacetyl group occurred only to the extent of 2-3%, and the D- and L-threo-1-(p-aminophenyl)-2-dichloroacetylamino-1,3-propandiols (X) which form can then be readily isolated in the form of pure hydrochlorides (yields 35-40%) and at the same time about 25% of the initial nitro compound (I) being recovered.

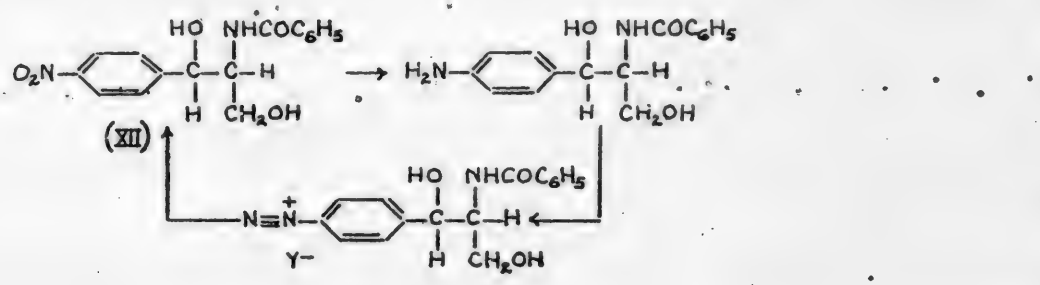
Diazotization of N-dichloroacetyl derivatives (X) is accomplished under the same conditions as with the N-benzoyl- compound (IV), but proceeds more rapidly. The diazonium salts of (IX) which result are more difficult to dissolve in water than salts of the original amines, and upon diazotizing concentrated solutions, they precipitate out. In the dry state these salts are very stable; thus, for example, the chlorides were stored in the dry state at room temperature for several weeks without noticeable decomposition. However, in aqueous solutions, diazonium salts of the type (XI) are more reactive than their benzoyl analogs (V), and it is, therefore, more expedient to carry out replacement of the diazo group in them at lower temperatures. It is true that yields of the chloromycetin analogs (VIII) formed are somewhat lower than the N-benzoyl derivatives (VI); thus, replacement of a diazo group by Cl, OH, and CN proceeds with a yield of 45-50%, and for AsO_3H_2 in only 16% yield. It is very intimately bound up with the fact that N-benzoyl derivatives (VI) crystallize better, and are more easily purified, than the N-dichloroacetyl derivatives (VIII).

To study the relation between structure and antibacterial activity for the chloromycetin series, it was of interest to obtain such compounds of the type (VIII) as those in which the nitro group is separated from the benzene ring of the chloromycetin molecule by a conjugated multiple bond system. Such compounds were synthesized by the authors from D- and L-threo-1-(p-aminophenyl)2-dichloroacetylamino-1,3-propandiols (X) by their condensation with p-nitrobenzaldehyde and p-nitronitrosobenzene, Schiff's bases (VIII; X = 4-$O_2NC_6H_4CH$ = N–) resulting in 62% yield, and nitroazo compounds (VIII; X = 4-$O_2NC_6H_4N$ = N–) in 56% yield. Furthermore, nitrohydroxyazo compounds (VIII; X = 3,4-$(O_2N)(HO)C_6H_3N$ = N–), obtained from D- and L-threo-amines (X), were synthesized by diazotization and subsequent coupling with o-nitrophenol (yield 29%).

It should be pointed out that despite relatively low yields, synthesis of chloromycetin analogs of the type (VIII), carried out according to Scheme 2, is very convenient because of the simplicity and brevity, since their synthesis is reduced to two stages: 1) the synthesis of amino compounds (X), and 2) their conversion via diazo compound or by condensation, to chloromycetin analogs of the type (VIII).

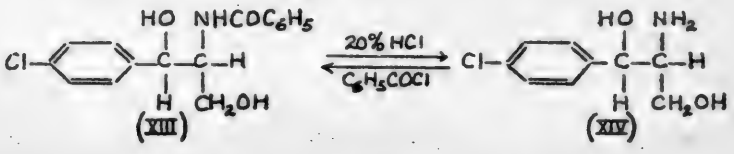
As was indicated above, it is imperative to have complete, accurate data concerning steric structures of the substances investigated in order to evaluate accurately the results of biological tests with chloromycetin analogs. It was necessary, in this regard, to determine whether the optically-active compounds of type (VIII), synthesized in accordance with Schemes 1 and 2, maintained the initial configuration, or whether in their formation there took place Walden inversion. The latter could only occur as a result of N ⟶ O^1-acyl migration in the diazotizing stages, which can be accomplished in both schemes, as well as during hydrolysis of the N-benzoyl group according to Scheme 1*.

In order to prove that no inversion occurs during the diazotization stage of Scheme 1, the authors reduced and diazotized L-threo-1-(p-nitrophenyl)2-benzoylamino-1,3-propandiol (XII), followed by replacement of the diazo group by the nitro group:



The original L-threo-nitro compound (XII) resulted, from which it follows that diazotization of threo-1-(p-aminophenyl)-2-benzoylamino-1,3-propandiols is not accompanied by inversion of their molecular configuration.

No inversion upon acid hydrolysis of the N-benzoyl derivatives of type (VI) was demonstrated by the authors for L-threo-1-(p-chlorophenyl)-2-benzoylamino-1,3-propandiol (XIII). Upon heating this compound with 20% HCl, the corresponding aminodiol (XIV) resulted, benzoylation of which lead to formation of the original L-threo- compound (XIII):



Hence, synthesis of chloromycetin analogs of the type (VII) as carried out by Scheme 1, was not accompanied by Walden inversion, and lead to compounds of the same configuration as existed for the original D- and

* It is known that under the influence of acid reagents, the N-acyl derivative of α-amino alcohols rearranges to salts of the corresponding O-acyl derivatives, and that this rearrangement may be accompanied by inversion in the configuration of that asymmetric carbon atom which is attached to the hydroxyl group. In a series of p-substituted threo-1-phenyl-2-acylamino-1,3-propandiols having the cis-configuration, the N ⟶ O^1-acyl migration usually takes place with preservation of the configuration [7], but isolated cases are known where in the course of this reaction inversion occurs [8].

L-threo-1-(p-nitrophenyl)-2-amino-1,3-propandiols (II).

Synthesis of type (VIII) compounds was carried out according to Scheme 2, which also took place with preservation of steric configuration for the molecules. This was demonstrated by the authors through conversion of L-threo-1-(p-aminophenyl)2-dichloroacetylamino-1,3-propandiol (X) into the p-chlorosubstituted analog of chloromycetin (VIII: X = Cl) belonging to the L-threo- series, and which was synthesized earlier according to Scheme 1 from L-threo-nitroaminodiol (II).

Inasmuch as synthesis of chloromycetin analogs according to Schemes 1 and 2 leads to formation of substances of strictly-defined configuration, it can be used as a method for proof of the steric structures for various compounds of the type (VIII) resulting from other procedures described in the literature. Thus, for example, the authors obtained corresponding racemates by combining the D- and L-isomers of p-chloro and p-iodo-substituted chloromycetin analogs (VIII: X = Cl or I) which were synthesized according to Schemes 1 and 2, and these racemates were found to be identical with racemic p-chloro and p-iodo-substituted chloromycetin analogs which were synthesized by proceeding from p-chloro- and p-iodo-acetophenones according to the method of Long and Troutman [9] published earlier. By the same fact was proved definitely for the first time that the Long and Troutman method applied to these compounds leads to chloromycetin analogs belonging to the threo- series.

EXPERIMENTAL

1. Benzoylation of D-, L- and D,L-threo-1-(p-Nitrophenyl)-2-amino-1,3-propandiols (II)

Benzoylation was carried out according to a method published earlier [5] for reacting aminodiols (II) with C_6H_5COCl in the presence of 0.5 N KOH solution and ether. If this reaction is carried out with continuous and very rigorous stirring of the mixture, then yields will reach 70-75%. The resulting substances were purified by crystallization from alcohol.

D-threo-III: m.p. 171-172°; $[\alpha]_D^{16} -120.5°$ (c 1.3 in CH_3OH). Found %: C 60.53; H 5.14; N 8.94. $C_{16}H_{16}O_5N_2$. Calculated %: C 60.75; H 5.10; N 8.86. L-threo-III: m.p. 171-172°; $[\alpha]_D^{17} +121.5°$ (c 2.1 in CH_3OH). D,L-threo-III, m.p. 162-163°.

2. Reduction of D-, L- and D,L-threo-1-(p-nitrophenyl)-2-benzoylamino-1,3-propandiols (III).

40 g of D-, L-, or D,L-threo-III in 300 ml of alcohol was hydrogenated in the presence of 5 g of nickel catalyst base. Reaction was carried out in a revolving autoclave (1 liter in volume) at 75-80° and an initial pressure of 40-50 atmospheres. After the cessation of H_2 absorption, the solution while hot was removed from catalyst by filtration and cooled. The resulting crystals were filtered off and washed with alcohol. The weight was 26.5-27.5 g. Another 6.5-7.0 g of substance was isolated from the mother liquor after evaporation. Total yield was 33-34.5 g (91-95%). The resulting amino compound was recrystallized from alcohol.

D-threo-IV: m.p. 170-171°; $[\alpha]_D^{16} -100.5°$ (c 1.1 in CH_3OH). L-threo-IV: m.p. 170-171°; $[\alpha]_D^{17} +99.5°$ (c 1.9 in CH_3OH). Found %: C 67.36; H 6.32; N 10.03. $C_{15}H_{18}O_3N_2$. Calculated %: C 67.14; H 6.34 N 9.79. D,L-threo-IV: m.p. 151-152°.

3. Diazotization of D- and of L-threo-1-(p-Aminophenyl)-2-benzoylamino-1,3-propandiols (IV), and Replacement of the Diazo Group in the Diazonium Salts (V)

a) L-threo-VI (X = H) Synthesis. 6 g of L-threo-IV was dissolved in 60 ml of 5% H_2SO_4 and diazotized at 0-5° with 20% $NaNO_2$ solution. The excess HNO_2 was decomposed with urea. 60 ml of alcohol and 6 ml of concentrated H_2SO_4 were added to the diazo solution, and 0.75 g of a copper-bronze added at 0-5°. After cessation of N_2 evolution the reaction mass was heated at 50-60° to complete decomposition of the diazonium salt (20-30 minutes), filtered and neutralized with 20% NaOH solution to a pH of 5.5-6.0. The reaction product was extracted with ethyl acetate, the alcohol having been distilled off in vacuo. The extract was washed with 5% NaOH solution and water, dried with Na_2SO_4, treated with carbon, with heat and evaporated to 10-12 ml volume. The precipitate which resulted upon cooling was filtered off and washed with ethyl acetate, and then with ether. Yield was 3.1 g (55%); m.p. 180-183°. The substance was purified by recrystallization from a mixture of alcohol and ethyl acetate (1:2).

L-threo-VI (X = H): m.p. 184-186°; $[\alpha]_D^{28} +98.9°$ (c 2.0 in CH_3OH). Found %: C 70.62; H 6.50; N 5.18. $C_{15}H_{17}O_3N$. Calculated %: C 70.83; H 6.32; N 5.16.

L-threo-VI (X = H) was synthesized from L-threo-IV via L-threo-V and by reduction of the latter with H_3PO_2; in this case, however, a more complex purification of the substance was necessary, which resulted in considerably lowered yield.

The L-threo-VI (X = H) O,O-diacetyl derivative was obtained by heating the corresponding diol with acetic anhydride and pyridine. After recrystallization from 50% alcohol, m.p. was 146-148°.

Found %: N 3.90. $C_{20}H_{21}O_5N$. Calculated %: N 3.94.

b) D- and L-threo-VI (X = Cl) Synthesis. 5 g of D- or L-threo-IV was suspended in 50 ml of 17% HCl, and was diazotized at 0-5° with 1.75 g of $NaNO_2$ solution in 7 ml of water. The excess HNO_2 was decomposed with urea. The diazo solution was added, with stirring, to Cu_2Cl_2 (prepared from 6 g of $CuSO_4 \cdot 5H_2O$ [10]) in 10 ml of 28% HCl solution precooled to 0°, and the reaction mass left at room temperature overnight. The precipitate formed was stirred and washed with water, dried and heated with 150 ml of ethyl acetate. The solution was filtered off, heated with carbon and evaporated to small volume. An almost pure chloro derivative crystallized out upon cooling. Yield was 4.0 g (75%); m.p. 170-171°. The substance was recrystallized from 50% alcohol.

D-threo-VI (X = Cl): m.p. 171-172°; $[\alpha]_D^{18} -102.8°$ (c 1.5 in CH_3OH). L-threo-VI (X = Cl): m.p. 171-172°; $[\alpha]_D^{18} +102.4°$ (c 4.5 in CH_3OH). Found %: C 62.96; H 5.51; N 4.63. $C_{18}H_{15}O_3NCl$. Calculated %: C 62.83; H 5.24; N 4.58.

In some cases, under the conditions described above, D- and L-threo-VI (X = Cl) were formed with m.p. 156° (instead of m.p. 171-172°). They had the same specific rotation value, and upon hydrolysis gave the same aminodiols as for compounds with m.p. 171-172°.

c) D-, L-, and D,L-threo-VI (X = I) Synthesis. 5 g of D-, L-, and D,L-threo-IV was dissolved in 165 ml of 1.5% H_2SO_4, 200 g of ice added, and diazotized at 0° with the theoretical quantity of 20% $NaNO_2$ solution. 4 g of KI in 50 ml of water was added, with cooling to 0°, and stirring, to the resulting diazo solution, and the reaction mixture left at 0° for 16 hours. The resins which separated were extracted with ethyl acetate (2 times in 75 ml portions) and the aqueous solution left at 20° to complete decomposition of the diazo compound, for which about 48 hours was required. The resulting precipitate was filtered off, washed with ethyl acetate, and dried; the weight was 4.0 g. The aqueous solution was extracted with ethyl acetate (3 times in 100 ml portions), and the extract washed with 5% $Na_2S_2O_3$ solution and water, followed by drying with Na_2SO_4 in the presence of carbon. The solution was evaporated in vacuo, the residue stirred with 10 ml of ethyl acetate and the precipitate filtered off; weight was 0.65 g. After recrystallization of the total resulting substance from 100 ml of 30% alcohol, there resulted 3.5 g (50%) of iodo derivative.

D-threo-VI (X = I): m.p. 178-179°; $[\alpha]_D^{22} -87.3°$ (c 0.5 in CH_3OH). L-threo-VI (X = I): m.p. 178-179°; $[\alpha]_D^{19} +86.2°$ (c 1.1 in CH_3OH). Found %: C 48.55; H 4.26; N 3.41. $C_{18}H_{16}O_3NI$. Calculated %: C 48.37; H 4.06; N 3.53. D,L-threo-VI (X = I): m.p. 173.5-174.5°. (The same substance was obtained from D- and L-threo-VI (X = I) by dissolving in and subsequently recrystallizing from 30% alcohol.

d) L-threo-VI (X = OH) Synthesis. 10 g of L-threo-IV was dissolved in 100 ml of 10% H_2SO_4 and diazotized at 0-5° with 2.5 g of $NaNO_2$ solution in 10 ml of water. The excess HNO_2 was decomposed with urea. The diazo solution was neutralized with $NaHCO_3$ to a pH of 5.5-6.0, heated at 70-90° to complete decomposition of the diazonium salt, decolorized with carbon, and cooled. 5 g of substance resulted (m.p. 183-185° with decomposition), which was recrystallized from 25% alcohol. Yield was 4 g (40%).

L-threo-VI (X = OH): m.p. 196-198° with decomposition; $[\alpha]_D^{19} +103°$ (c 2.1 in CH_3OH). Found %: C 67.06; H 6.00; N 5.10. $C_{16}H_{17}O_4N$. Calculated %: C 66.88; H 5.99; N 4.88.

e) D- and L-threo-VI (X = CN) Synthesis. 25 g of D- or L-threo-IV was dissolved in 250 ml of 5% H_2SO_4 and diazotized at 0-5° with 6.25 g of $NaNO_2$ solution in 25 ml of water. The diazo solution was neutralized with $NaHCO_3$ to a pH of 6.0-6.5, and gradually added with stirring to a cuprous cyanide solution* which was under a layer of toluene (250 ml) and precooled to −5°. After completion of the diazonium salt decomposition, the reaction mass was stirred for another 15 minutes and separated from the resinous substance which came out by filtration. The toluene layer was separated and the aqueous solution extracted with ethyl acetate (4 times in 75 ml portions). The extract was dried with Na_2SO_4, evaporated to 40-50 ml volume and diluted with 5 times the volume of benzene; 4.7 g of nitrile precipitated, with m.p. 136-137.5°. The resinous substance filtered off from the reaction mass was dissolved in ethyl acetate, the solution clarified with carbon, and the solvent distilled off. The residue, when stirred with benzene, crystallized. It was heated with water (3 times in 500 ml portions) and the hot, aqueous solution filtered off and left overnight; the oily substance which separated was purified by repeating the described treatment with boiling water. The combined water solution was decolorized by heating with carbon and then extracted with ethyl acetate

* The latter was obtained by mixing 55 g of KCN solution in 110 ml of water with a suspension of Cu_2Cl_2 (from 63 g of $CuSO_4 \cdot 5H_2O$ [10]) in 100 ml of water, and by neutralizing the solution formed with 10% CH_3COOH to a pH of 7.0-7.5.

(3 times in 150 ml portions). The extract was evaporated to 75-100 ml volume and diluted with 5 times the volume of benzene. 16.4 g of almost pure nitrile resulted, with m.p. 136-137.5°. The total yield was 21.1 g (82%). The substance was recrystallized from water.

D-threo-VI (X = CN): m.p. 139-140°; $[\alpha]_D^{20}$ −130.4° (c 5.2 in CH_3OH). L-threo-VI (X = CN): m.p. 139-140°; $[\alpha]_D^{20}$ + 129.8° (c 5.2 in CH_3OH). Found %: C 69.05; H 5.74; N 9.57. $C_{17}H_{12}O_3N_2$. Calculated %: C 68.92; H 5.46; N 9.46.

f) L-threo-VI (X = NO_2) Synthesis. 2.8 g of L-threo-IV was dissolved in 14 ml of 10% H_2SO_4 and diazotized at 0-5° with 20% $NaNO_2$ solution. The diazo solution was neutralized with $CaCO_3$ to disappearance of an acid reaction to Congo red, and filtered. 1.5 g of $Na_3Co(NO_2)_6$ was dissolved in the filtrate at room temperature and the solution cooled to 3-5°. After 15 minutes the liquid was decanted off from the precipitate which formed, and a suspension of 0.4 g Cu_2O in a solution of 1 g of $NaNO_2$ and 1 g of $CuSO_4 \cdot 5H_2O$ in 6 ml of water added with cooling and stirring. After cessation of N_2 evolution, stirring was stopped and the reaction mass left for 10-12 hours. The nitro compound extracted with ethyl acetate (7-8 times with 30 ml portions), the extract washed with 3% H_2SO_4, 5% $NaHCO_3$ solution, water, and then dried with Na_2SO_4, clarified with charcoal, and concentrated. The residue was heated with 15 ml of water, the aqueous solution treated with carbon while heating, and then cooled. The resulting precipitate was purified by recrystallization from water with charcoal, and then with 20% alcohol. The resulting nitro compound had a m.p. of 169-170° and $[\alpha]_D^{20}$ + 122° (c 1.3 in CH_3OH); it was identical with L-threo-III described in Experiment 1.

g) L-threo-VI (X = AsO_3H_2) Synthesis. 5 g of L-threo-IV was dissolved in 165 ml of 1.5% H_2SO_4 and diazotized at 0-5° with 1.25 g of $NaNO_2$ solution in 5 ml of water. The excess of NHO_2 was decomposed with urea. The diazo solution was neutralized with $NaHCO_3$ to a pH of 6.5, and 0.1 g of $CuSO_4 \cdot 5H_2O$, 2.2 g As_2O_3 and 4.4 g of Na_2CO_3 in 16 ml of water added dropwise over a period of 3 hours to the solution, with stirring, at 15°. The reaction mixture was stirred for another hour or more, filtered, neutralized with concentrated HCl to a pH of 7, evaporated in vacuo, and then filtered again. The filtrate (5-7 ml) was gradually acidified with concentrated HCl to an acid reaction with Congo red, whereby resins separated at first, which were filtered off, after which the precipitate of arsonic acid (1.88 g) separated. After recrystallization from 30% alcohol, the yield was 1.53 g (22%).

L-threo-VI (X = AsO_3H_2) decomp. 142-143°; $[\alpha]_D^{22}$ + 88.5° (c 2.1 in CH_3OH). Found %: As 18.45; N 3.28. $C_{15}H_{18}O_6NAs$. Calculated %: As 18.95; N 3.54.

h) L-threo-VI (X = 1-[2-(HO)$C_{10}H_5$]N = N−) Synthesis. 2 g of L-threo-IV was dissolved in 20 ml of 5% H_2SO_4 and diazotized at 0-5° with 0.5 g of $NaNO_2$ solution in 1.5 ml of water. The excess HNO_2 was decomposed with urea. The diazo solution was added, with stirring, to 1.3 g of β-naphthol solution precooled to 0°, plus 0.36 g of NaOH and 1.5 g of Na_2CO_3 in 40 ml of water. The resulting red precipitate was filtered off and washed with water, followed by methanol. The yield was 2.6 g (84 %). The substance was purified by recrystallization from a large volume of methanol.

L-threo-VI (X = 1-[2-(HO)$C_{10}H_5$]N = N−): decomposition point 224-226°; $[\alpha]_D^{18}$ + 180° (c 0.3 in dioxane). Found %: C 70.39, H 5.43; N 9.83. $C_{25}H_{23}O_4N_3$. Calculated %: C 70.75; H 5.21; N 9.52.

4. Hydrolysis of p-Substituted D- and L-threo-1-Phenyl-2-benzoylamino-1,3-propandiols (VI)

a) D- and L-threo-VI (X = Cl) Hydrolysis. 2.5 g of D- or L-threo-VI (X = Cl) was heated for 4 hours with 25 ml of 20% HCl. Benzoic acid was extracted with ether, the aqueous solution heated with carbon and evaporated in vacuo to dryness. The residue was dissolved in 3 ml of water and concentrated NH_3 solution added. The base which separated was recrystallized with charcoal from 15 ml of water. 0.92 g (56%) of pure aminodiol resulted.

D-threo-VII (X = Cl): m.p. 145-147°; $[\alpha]_D^{28}$ −33.6° (c 2.5 in 5% HCl). L-threo-VII (X = Cl): m.p. 145-147°; $[\alpha]_D^{20}$ + 35.0° (c 4.0 in 5% HCl). Found %: C 53.75; H 6.22; N 6.86. $C_9H_{12}O_2NCl$. Calculated%: C 53.60; H 6.01; N 6.95. D,L-threo-VII (X = Cl): m.p. 122-123°, (this compound was prepared from D- and L-threo-VII (X = Cl) by combining and then recrystallizing from water).

0.2 g of L-threo-VII (X = Cl) was benzoylated under the conditions of Experiment 1. 0.2 g (66%) of L-threo-VII (X = Cl) resulted, identical with the substance which was described in Experiment 3b.

b) D-, L- and D,L-threo-VI (X = I) Hydrolysis. 3.5 g of D-, L- or D,L-threo-VI (X = I) was heated for 10 hours with 35 ml of 10% HCl. The solution was clarified by heating with carbon and after extraction of benzoic acid with ether, concentrated NH_3 solution was added. The oily substance which separated was extracted with ethyl acetate, the extract heated with carbon, dried with Na_2SO_4, and evaporated in vacuo. The residue was mixed with a small

volume of ethyl acetate, the resulting precipitate filtered off, and washed with the same solvent. Yield was 1.42 g (55%). The D- and L-isomers were recrystallized from 15% alcohol, and the D,L-compound recrystallized from water.

D-threo-VI (X = I): m.p. 103-104°. L-threo-VI (X = I): m.p. 103-104°; $[\alpha]_D^{28}$ + 23.6° (c 1.9 in 5% HCl). Found %: C 36.56; H 4.14; N 4.14; N 4.31. $C_9H_{12}O_2NI$. Calculated %: C 36.87; H 4.09; N 3.78. D,L-threo-VII (X = I): m.p. 180-181°.

c) D- and L-threo-VI (X = CN) Hydrolysis. 15 g of D- or L-threo-VI (X = CN) was boiled for 8 hours with 225 ml of 20% HCl. The benzoic acid was extracted with ether, the aqueous solution heated with carbon, and the solution evaporated in vacuo to dryness. The residue was dissolved in 20 ml of water, the solution neutralized with concentrated NH_3 solution to pH 5-6, and the resulting precipitate filtered off. The weight was 4.6 g. An equal volume of concentrated HCl was added to the filtrate, the solution boiled for 8 hours, and treated as described above. Another 2.4 g was obtained. The total yield was 7.0 g (65%). The substance was recrystallized from 280 ml of water and the solution partially evaporated before cooling.

D-threo-VII (X = COOH): decomposition point was 348-349° – the capillary being placed in the block at 320°; $[\alpha]_D^{22}$ −32.4° (c 4.0 in 5% HCl). L-threo-VII (X = COOH); decomp. pt. 348-349°; $[\alpha]_D^{22}$ + 32.8° (c 4.0 in 5% HCl). Found %: C 56.37; H 6.49; N 6.60. $C_{10}H_{13}O_4N$. Calculated %: C 56.87; H 6.16; N 6.63.

These substances were found to be internal salts. They are insoluble in organic solvents, poorly soluble in water, and readily soluble in aqueous solutions of acid and of alkali; they do not undergo N-dichloroacetylation upon heating with $Cl_2CHCOOCH_3$, but they can be N-acylated by reacting with $Cl_2CHCOCl$ in the presence of an aqueous solution of K_2CO_3.

5. Dichloroacetylation of p-Substituted D- and L-threo-1-Phenyl-2-amino-1,3-propandiols (VII)

a) D- and L-threo-VIII (X = Cl) Synthesis. 2.7 g of D- or L-threo-VII (X = Cl) and 2.9 g of $Cl_2CHCOOCH_3$ were heated to 90° and kept at this temperature for 5 minutes after dissolution of the substance. The viscous mass was stirred with heptane (3 times in 5 ml portions), dissolved in 2-3 ml of dichloroethane, and after adding 3 ml of heptane, was left overnight. Another 3-5 ml of heptane was added to the resulting precipitate, the precipitate filtered off and recrystallized from dichloroethane, and then from water. The yield was 1.95 g (47%).

D-threo-VIII (X = Cl): m.p. was 92-93°; $[\alpha]_D^{23}$ + 8.2° (c 7.1 in CH_3OH). L-threo-VIII (X = Cl): m.p. 92-93°; $[\alpha]_D^{17}$ −9.0° (c 3.5 in CH_3OH). Found %: C 42.41; H 4.06; N 4.49. $C_{11}H_{12}O_3NCl_3$. Calculated %: C 42.26; H 3.87; N 4.48. D,L-threo-VIII (X = Cl): m.p. 119-120° (this compound being prepared from D- and L-threo-VIII (X = Cl) by combining them and then recrystallizing from water).

b) D- and L-threo-VIII (X = I) Synthesis. 0.5 g of D- or of L-threo-VII (X = I) and 0.4 g of $Cl_2CHCOOCH_3$ were heated for 15 minutes at 95°, and kept at this temperature for 5 minutes. The reaction mass was cooled and stirred with 5 ml of heptane. The precipitate was filtered off, washed with heptane, and recrystallized from water. The yield was 0.5 g (73%).

D-threo-VIII (X = I): m.p. 103-104°; $[\alpha]_D^{22}$ + 9.7° (c 3.5 in CH_3OH). L-threo-VIII (X = I): m.p. 103-104°; $[\alpha]_D^{17}$ −10.8° (c 3.5 in CH_3OH). Found %: C 32.41; H 2.99; N 3.57. $C_{11}H_{12}O_3NCl_2I$. Calculated %: C 32.68; H 2.97; N 3.46. D,L-threo-VIII (X = I): m.p. 122-123° (this compound being prepared from D- and L-threo-VIII (X = I) by combining them and then recrystallizing from water).

c) D- and L-threo-VIII (X = COOH) Synthesis. 60 ml of ether was added to a solution of 4 g of D- or L-threo-VII (X = COOH) and 30 g of K_2CO_3 in 60 ml of water. The mixture was cooled to −5°, and 16 g of $Cl_2CHCOCl$ solution in 30 ml of absolute ether added with stirring for 2 hours. The reaction mass was filtered off, acidified with 20% HCl to a pH of 4-4.5, and extracted repeatedly with ethyl acetate. The unreacted aminodiol which separated during extraction was filtered off, washed with water, and dried. Weight was 2.3 g. The ethyl acetate solution was evaporated to dryness in vacuo. 1.85 g of pure substance resulted; yield was 71% (calculating on the basis of unreacted aminodiol). The substance was crystallized from water.

D-threo-VIII (X = COOH): m.p. 190-191°; $[\alpha]_D^{25}$ + 12.0° (c 3.5 in CH_3OH). L-threo-VIII (X = COOH): m.p. 190-191°; $[\alpha]_D^{20}$ −13.9° (c 5.3 in CH_3OH). Found %: C 44.55; H 4.00; N 4.48. $C_{12}H_{13}O_5NCl_2$. Calculated %: C 44.74; H 4.08; N 4.35. D,L-threo-VIII (X = COOH): m.p. 188-189° (this compound being prepared from D- and L-threo-VIII (X = COOH) by combining them and subsequently recrystallizing from water).

6. Synthesis of D- or of L-threo-1-(p-Aminophenyl)-2-dichloroacetylamino-1,3-propandiols (X)

a) D- and L-threo-II Reduction. 50 g of D- or L-threo-II in 350 ml of alcohol was hydrogenated in the presence of 10 g of nickel catalyst base. Reaction was carried out in a revolving autoclave (of 1 liter volume) at 75-80° at an initial pressure of 40-50 atmosphere. While hot, the solution was removed from catalyst by filtration, evaporated in vacuo to the beginning of crystallization, and cooled. The resulting crystals were filtered off and washed with alcohol. Weight was 28-29 g. 10.5-11 g of substance was isolated after evaporation from mother liquor. Total yield was 39-39.5 g (90-92%). The resulting diamino compound was recrystallized from alcohol.

D-threo-IX: m.p. 135-136°; $[\alpha]_D^{22}$ −28.8° (c 9.4 in CH_3OH). L-threo-IX: m.p. 135-136°; $[\alpha]_D^{20}$ + 27.5° (c 10.2 in CH_3OH). Found %: C 59.45; H 7.82; N 15.35. $C_9H_{14}O_2N_2$. Calculated %: C 59.34; H 7.77; N 15.38.

b) D- and L-threo-IX Dichloroacetylation. 15 g of D- or L-threo-IX was dissolved in 150 ml of absolute methanol in 30 ml of $Cl_2CHCOOCH_3$ purified by pyridine. The mixture was left at 18-23° for 24 hours. The solvent and $Cl_2CHCOOCH_3$ excess were distilled off completely in vacuo at 25-30°, and the residue stirred with ethyl acetate (6 times in 50 ml portions). The solution was left for 1-2 hours, filtered off from the resins which formed, washed with water (4 times in 50 ml portions) and dried with Na_2SO_4 overnight at 0-5°, and evaporated in vacuo to a volume of 50-60 ml. The HCl solution in absolute methanol was added, the resulting precipitate filtered off, and washed, first with methanol, and then with ether. For purification, the substance was dissolved in 6 times the volume of absolute methanol and absolute ether added; a crystalline precipitate gradually formed. Yield was 6.7 g (25%). The hydrochloride of the amino compounds (X) gradually decomposed without melting upon heating.

D-threo-X hydrochloride: $[\alpha]_D^{18}$ + 8.1° (c 9.6 in CH_3OH). L-threo-X hydrochloride: $[\alpha]_D^{20}$ −8.5° (c 5.3 in CH_3OH). Found %: C 39.94; H 4.79; N 8.63. $C_{11}H_{15}O_3N_2Cl_3$. Calculated %: C 40.06; H 4.69 N 8.50.

c) D- and L-threo-I Reduction. 15 g of D- or L-threo-I in 180 ml of alcohol was hydrogenated in the presence of 7.5 g of nickel catalyst base at normal pressure and 18-20°. Reduction was stopped after absorption of one-half of the theoretical volume of hydrogen. The solution was filtered, evaporated in vacuo at 20-25° to a volume of 50 ml, and then an alcoholic solution of HCl added to it. A crystalline precipitate resulted upon gradual addition of ether (200 ml), which was filtered off and washed with alcohol-ether mixture. 5.5-6.0 g (36-39%) of D- or of L-threo-X hydrochloride resulted. The mother liquor was evaporated in vacuo to a small volume, diluted with water and extracted with ethyl acetate. The extract was dried with Na_2SO_4 and evaporated in vacuo. The residue was stirred with ethyl acetate and filtered. 3.5-4.0 g (23-27%) of initial nitro compound (I) resulted, with m.p. 150-151° (from water).

7. Diazotization of D- and L-threo-1-(p-Aminophenyl)-2-dichloroacetylamino-1,3-propandiols (X) and Replacement of the Diazo Group of Diazonium (XI) Salts

a) D- and L-threo-XI (Y = Cl) Synthesis. 3 g of D- or L-threo-X hydrochloride was dissolved in 16.5 ml of 5% HCl and diazotized at 0° with 0.63 g of $NaNO_2$ solution in 3 ml of water. The resulting diazonium salt precipitate was filtered off, washed with water, and dried. Yield was 1.35 g (44%). Upon heating, the substance decomposed without melting.

D-threo-XI (Y = Cl): $[\alpha]_D^{19}$ + 9.5° (c 5.1 in 1% HCl). L-threo-XI (Y = Cl): $[\alpha]_D^{17}$ −9.8° (c 5.1 in 1% HCl). Found %: Cl^- 10.38. $[C_{11}H_{12}O_3N_3Cl_2]^+Cl^-$. Calculated %: Cl^- 10.41.

b) L-threo-VIII (X = Cl) Synthesis. 1 g of L-threo-X hydrochloride was dissolved in 15 ml of 5% HCl and was diazotized at 0-5° with 0.21 g of $NaNO_2$ solution in 1 ml of water. The diazonium salt was added with stirring to Cu_2Cl_2 solution (prepared from 4 g of $CuSO_4 \cdot 5H_2O$ [10]) in 15 ml of 28% HCl, precooled to −5°. After completion of the diazo compound decomposition, the reaction mixture was extracted with ethyl acetate (3 times in 10 ml portions). The extract was washed with water, dried with Na_2SO_4, and evaporated in vacuo. The residue was dissolved in dichloroethane and heptane gradually added to the solution, whereupon resins first isolated were filtered off, and the L-threo-VIII (X = Cl) then precipitated out. Yield was 0.43 g (45%). After recrystallization from water in the presence of charcoal, the m.p. was 92-93°. The substance did not give depression in melting point when mixed with L-threo-VIII (X = Cl) which was synthesized according to Scheme 1.

c) Synthesis of D- and of L-threo-VIII (X = OH). 3 g of D- or of L-threo-X hydrochloride was dissolved in 30 ml of water, 9 ml of 10% H_2SO_4 added, and if needed, the solution was clarified in the cold with charcoal and then diazotized at 0-5° with 0.66 g of $NaNO_2$ solution in 3 ml of water. The HNO_2 excess was decomposed with urea. The diazo solution was then neutralized with $NaHCO_3$ to a pH of 5.5 and then heated at 70-90° to the complete decomposition of diazonium salt. The solution was filtered, heated with carbon, and extracted with ethyl

acetate. The extract was dried with Na_2SO_4 and evaporated in vacuo. The residue was stirred with ethyl acetate, filtered off, and recrystallized from ethyl acetate. Yield was 1.4 g (52%).

D-threo-VIII (X = OH): m.p. 160-161° (with decomposition); $[\alpha]_D^{19}$ −8.1° (c 7.8 in CH_3OH). L-threo-VIII (X = OH): m.p. 160-161° (with decomposition); $[\alpha]_D^{19}$ + 7.8° (c 10.9 in CH_3OH). Found %: N 91; Cl 23.96. $C_{11}H_{13}O_4NCl_2$. Calculated %: N 4.76; Cl 24.13. D,L-threo-VIII (X = OH): m.p. 138-140° (this compound having been prepared from D- and L-threo-VIII (X = OH) by mixing them and subsequently recrystallizing from ethyl acetate).

d) D- and L-threo-VIII (X = CN) Synthesis. 5 g of D- or of L-threo-X was dissolved in 50 ml of water, 15 ml of 10% H_2SO_4 then added, and the solution diazotized at 0-5° with 1.1 g of $NaNO_2$ solution in 4 ml of water. The diazo solution was neutralized with $NaHCO_3$ to a pH of 6.5-7.0, and gradually, with stirring, it was added to a solution of cuprous cyanide under a toluene layer (25 ml) and precooled to −7°.* After completion of diazonium salt decomposition, the reaction mixture was stirred for another 10 minutes and extracted with ethyl acetate (5 times in 40 ml portions). The extract was dried with Na_2SO_4, evaporated to dryness in vacuo, and treated with boiling water (4 times with 50 ml portions). The aqueous solution was heated with charcoal and evaporated in vacuo to 35-40 ml volume. After cooling, there resulted almost pure nitrile. A small amount of substance was again isolated after evaporation of the mother liquor. Yield was 2.4 g (52%). The resulting nitrile was recrystallized with water.

D-threo-VIII (X = CN): m.p. 135.5-136.5°; $[\alpha]_D^{22}$ + 15.4° (c 17.9 in CH_3OH). L-threo-VIII (X = CN): m.p. 135.5-136.5°; $[\alpha]_D^{20}$ −17.0° (c 8.7 in CH_3OH). Found %: C 47.81; H 4.05; N 9.25. $C_{12}H_{12}O_3N_2Cl_2$. Calculated %: C 47.54; H 4.00; N 9.24. D,L-threo-VIII (X = CN): m.p. 132.5-133.5° (this compound having been prepared from D- and L-threo-VIII (X = CN) by mixing them and subsequently crystallizing them from water).

0.3 g of L-threo-VIII (X = CN) was hydrolyzed under conditions of Experiment 4c. 0.16 g (76%) of L-threo-VII (X = COOH) was isolated, identical with the substance obtained in Experiment 4 c.

e) D- and L-threo-VIII (X = AsO_3H_2) Synthesis. 7 g of the hydrochloride of D- or of L-threo-X was dissolved in 230 ml of 1.5% H_2SO_4, and when needed, the solution was clarified with charcoal in the cold and diazotized at 0-5° with 1.6 g of $NaNO_2$ solution in 5 ml of water. The excess HNO_2 was decomposed with urea and the diazo solution was added over a period of 2 hours, dropwise, to a stirred solution of 0.12 g of $CuSO_4 \cdot 5H_2O$, 2.75 g of As_2O_3 and 5.5 g of Na_2CO_3 in 25 ml of water at 15°. The reaction mixture was stirred for another hour, filtered, acidified with concentrated HCl to a pH of 6.5, evaporated in vacuo, and then filtered again. The filtrate (7-10 ml) was gradually acidified with concentrated HCl to an acid reaction with Congo red, whereupon resins first separated, which were filtered off. After addition of ethyl acetate to the solution, at the boundary layer gradual formation of crystals took place. After 10-12 hours, the precipitate was filtered off, washed with ethyl acetate and dried. The dry substance was heated with 15 ml of alcohol, the solution filtered, and evaporated to dryness in vacuo. The residue was mixed with ethyl acetate and the precipitate filtered off. Weight was 2.2 g. The substance was dissolved in 2 times the volume of hot absolute alcohol and precipitated with ethyl acetate, whereupon a crude product first separated, and then the pure arsonic acid. Yield was 1.36 g (16%). The substance did not possess a sharp melting point.

D-threo-VIII (X = AsO_3H_2): $[\alpha]_D^{20}$ + 8.6° (c 7.8 in CH_3OH). L-threo-VIII (X = AsO_3H_2): $[\alpha]_D^{22}$ −7.8° (c 7.9 in CH_3OH). Found %: As 18.09; N 2.91. $C_{11}H_{16}O_6NCl_2As$. Calculated %: As 18.64; N 3.48.

f) D- and L-threo-VIII [X = 3,4-$(NO_2)(HO)C_6H_3N=N-$] Synthesis. 6 g of D- or of L-threo-X hydrochloride was dissolved in 80 ml of 2.5% HCl, clarifying if necessary in the cold with charcoal, and diazotized at 0 to −5° with 1.4 g of $NaNO_2$ solution in 7 ml of water. Excess HNO_2 was decomposed with urea. The diazo solution was poured into 2.8 g of o-nitrophenol, 7.3 g of NaOH and 3.5 g of Na_2CO_3 dissolved in 65 ml of water at 0 to −5°, and stirred at 15-20° for 2 hours, and acidified with 5% HCl to an acid Congo red reaction. After standing for 12 hours at 0 to −5°, the resulting resinous substance solidified, was stirred, washed with water, and dried. The azo compound was extracted repeatedly with boiling dichloroethane and was precipitated with double the volume of heptane, after which it was recrystallized from 30% CH_3COOH. Yield was 2.3 g (29%).

D-threo-VIII [X = 3,4-$(NO_2)(HO)C_6H_3N=N-$]: m.p. 157-159°; $[\alpha]_D^{22}$ + 21.2° (c 5.3 in CH_3OH). L-threo-VIII [X = 3,4-$(NO_2)(HO)C_6H_3N=N-$]: m.p. 157-159°; $[\alpha]_D^{16}$ −22.0° (c 7.5 in CH_3OH). Found %: N 12.33. $C_{17}H_{16}O_6N_4Cl_2$. Calculated %: N 12.64. D,L-threo-VIII [X = 3,4-$(NO_2)(HO)C_6H_3N=N-$]: m.p. 153-155° (this compound was prepared from D- and L-threo-VIII [X = 3,4-$(NO_2)(HO)C_6H_3N=N-$] by combining them,

* The latter was obtained by mixing 10 g of KCN solution in 20 ml of water with Cu_2Cl_2 suspension (from 12 g of $CuSO_4 \cdot 5H_2O$ [10]) in 20 ml of water, and neutralizing the resulting solution with a 10% solution of CH_3COOH to a pH of 7.0-7.5.

followed by their recrystallization from dichloroethane).

8. Condensation of D- and of L-threo-1-(p-Aminophenyl)-2-dichloroacetylamino-1,3-propandiols (X) with p-Nitronitrosobenzene and p-Nitrobenzaldehyde

a) D- and L-threo-VIII (X = p-$NO_2C_6H_4N$ = N−) Synthesis. 2.3 g of D- or of L-threo-X hydrochloride solution in 15 ml of methanol was mixed with 0.8 g anhydrous CH_3COONa in 10 ml of methanol, filtered, cooled to 5° and a solution of 0.95 g of p-nitronitrosobenzene in 15 ml of CH_3COOH added. After 10-12 hours, the resulting crystals of p,p'-dinitroazoxybenzene were filtered: weight 0.13 g, m.p. 191-192° (from CH_3COOH) [11]. The filtrate was evaporated in vacuo, the residue stirred with benzene, filtered off, washed with methanol and crystallized from ethyl alcohol. Yield was 1.48 g (58%).

D-threo-VIII (X = p-$NO_2C_6H_4N$ = N−): m.p. 173-174°; $[\alpha]_D^{20}$ −62.2° (c 0.6 in acetone). L-threo-VIII (X = p-$NO_2C_6H_4N$ = N−): m.p. 173-174°; $[\alpha]_D^{20}$ + 64.9° (c 0.8 in acetone). Found %: C 48.04; H 3.39; N 13.30. $C_{17}H_{16}O_5N_4Cl_2$. Calculated %: C 47.79; H 3.77; N 13.11. D,L-threo-VIII (X = p-$NO_2C_6H_4N$ = N−): m.p. 171-172° (this compound having been prepared from D- and from L-threo-VIII (X = p-$NO_2C_6H_4N$ = N−) by mixing them and recrystallizing from alcohol.

b) D- and L-threo-VIII (X = p-$NO_2C_6H_4CH$ = N−) Synthesis. 2 g of D- or of L-threo-X hydrochloride and 0.9 g of p-nitrobenzaldehyde were dissolved in 25 ml of methanol and mixed with a solution of 1.2 g of CH_3COOK (anhydrous) in 25 ml of methanol. The reaction mixture was left for 1 hour at 15-20°, was then heated to boiling, 95 ml of hot water added to it, and the solution heated with charcoal. After cooling, the resulting precipitate was filtered off, washed with methanol and dried. Yield was 1.6 g (62%). The substance was recrystallized from ethyl alcohol.

D-threo-VIII (X = p-$NO_2C_6H_4CH$ = N−): m.p. 164-166° with decomposition; $[\alpha]_D^{20}$ −18.8° (c 3.6 in dioxane). L-threo-VIII (X = p-$NO_2C_6H_4CH$ = N−): m.p. 165-167° with decomposition; $[\alpha]_D^{20}$ + 19.7° (c 2.5 in dioxane). Found %: C 50.62; H 4.01; N 9.75. $C_{12}H_{17}O_5N_3Cl_2$. Calculated %: C 50.72; H 4.03; N 9.85. D,L-threo-VIII (X = p-$NO_2C_6H_4CH$ = N−): m.p. 155-157° with decomposition. (This compound was obtained from D- and L-threo-VIII (X = p-$NO_2C_6H_4CH$ = N−) by combining them, followed by recrystallization from alcohol).

SUMMARY

Two general synthetic methods have been developed for optically-active chloromycetin (levomycetin) analogs of the type:

p-$XC_6H_4CHOHCH(NHCOCHCl_2)CH_2OH$.

Both methods of synthesis make it possible to start with compounds of known steric configuration which do not change during the process of synthesizing the analogs indicated.

By these procedures, chloromycetin analogues of the D- and L-threo-series, which have X = Cl, I, OH, CN, COOH, AsO_3H_2, 4-$NO_2C_6H_4CH$ = N−, 4-$NO_2C_6H_4N$ = N− and 3,4-$(NO_2)(HO)C_6H_3N$ = N−, have been synthesized.

The synthetic procedures which have been developed may be used to prove the steric structures of certain types of chloromycetin analogs obtained by the methods of other investigators and which are described in the literature. It has been demonstrated that the method of Long and Troutman, published previously, leads, in a number of cases, to chloromycetin analogs belonging to the threo-series.

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RESEARCH IN THE FIELD OF CONJUGATED SYSTEMS

LII. CONCERNING THE SEQUENCE OF BROMINE ADDITION TO VINYLALKYLACETYLENES

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Compounds with conjugated double and triple bonds (eninic systems) possess a number of specific peculiarities which distinguish them from compounds containing conjugated double bonds.

The simplest member of the eninic systems —vinylacetylene— is capable of a hydrogen atom replacement by metals, and of various condensations at the expense of this hydrogen, as well as of addition reactions of water, alcohols and acids (under conditions of the Kucherov reaction) at the acetylenic bond [1]. None of these reactions is characteristic for divinyl. On the other hand, vinylacetylene, in contrast to divinyl, almost fails to enter into homo- and hetero-cyclization reactions (dienic syntheses), apparently because of steric hindrances (linear placement of the three carbon atoms). Similar distinctions can also occur with homologs of these two hydrocarbons.

The vinylacetylene addition reaction attests to the high reactivity of the first carbon atom in the molecule. Hydrogen halides add to it in the 1,4-position, with formation of the allene halogenides which, under influence of catalysts, readily rearrange to diene halogenides (allene-dienic isomerization with change in the halogen position). The latter substances are formed directly as the result of addition of hydrogen halides in the presence of catalyst which promotes the isomerization[2].

As experiments by one of us with Sopov [3] have demonstrated, bromine adds to vinylacetylene chiefly at the 1,2-, but also at the 1,4-position. 1,4-Dibromide is capable of rearrangement to 1,2-dibromide with conjugated double bonds, in the presence of catalysts. Among the products of this reaction a third isomer was also present —acetylene dibromide, but its amount was quite small.

According to the literature data, vinylacetylene homologs with a radical in the first position behave analogously to vinylacetylene. Thus, an investigation of their reaction with hydrogen chloride did not evidence any peculiarities as compared with vinylacetylene [4].

The experiments set up for bromination of vinylalkylacetylenes led to unexpected results: bromine addition took place almost exclusively at the double bond (3,4-position).

It might be expected that the following three dibromides (I), (II) and (III) would be formed from the addition of bromine to vinylacetylene homologs

$$R-CBr=CBr-CH=CH_2; \qquad R-C\equiv C-CHBr-CH_2Br; \qquad R-CBr=C=CH-CH_2Br.$$

(I) (II) (III)

In actuality, substances with very narrow boiling range resulted, having the following properties:

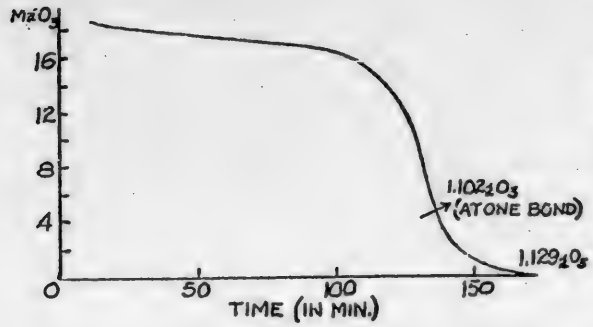
1) Upon oxidation with permanganate and by ozonization, they form α,β-dibromopropionic acid, along with the corresponding carboxylic acid from the second part of the molecule (the first homolog giving acetic acid, and the second propionic acid). With ozonization, only one molecule of ozone is absorbed. The ozonization rate curve does not possess inflexions, which indicates the presence of only one multiple bond (see Figure).

2) Upon reaction with alcoholic alkali in the cold, they immediately split out one hydrogen bromide molecule, with formation of the monobromides of the vinylacetylene series.

3) When stored for several months, they do not polymerize.

4) When reacted with Cu_2Br_2 + HBr, they convert readily to dienic dibromides, stable to alkali, and polymerizing upon storage, exposure to light, and with heating.

5) 2240 cm^{-1} (intense) and 2347 cm^{-1} (faint) are found for the combined dispersion spectrum of dibromide prepared from hexenine, which are characteristic for a triple bond between the 2 and 3 carbon atoms. In the spectrum for its isomerization product —diene dibromide— there is found an intense frequency at 1611cm^{-1} for the double bond. There are no frequencies for the triple bond.



None of these properties coincides with Formulas (I) or (III), which makes it possible to ascribe, without hesitation, Formula (II) to the dibromides obtained.

Along with the main fraction of dibromides, there usually results in addition lower fractions; however, their amount is small and does not constitute more than 10% of the main fraction. Apparently diene dibromides are contained in these lower fractions, since they give a high refractive index and upon storage resinify readily.

The residue from distillation of the dibromides contains tetrabromides. The latter were not isolated in pure state: they decompose somewhat upon distillation in vacuo.

The acetylene dibromides (II) were slightly yellow liquids with a pine odor, somewhat irritating. They possessed slightly higher boiling points as compared with the corresponding halogen derivatives (1,2-dibromopentane had a b.p. of 68°, 1,2-dibromohexane 82°, 1,2-dibromoheptane 98-99° at 12 mm, 1,2-dibromooctane 118.5° at 15 mm). With increase in alkyl, this difference decreases somewhat. For all of the dibromides the molecular refraction values found are higher than calculated. This phenomenon exists for other unsaturated bromides of the allyl type. Within a homologous series of dibromides, specific gravity decreases and refractive index decreases, according to the rule. The most important constants for acetylene dibromides are given in Table 1.

TABLE 1

Substance	Boiling point at 10 mm (in °)	d_4^{20}	n_D^{20}	MR_D	
				Found	Calculated
$CH_2Br-CHBr-C\equiv C-CH_3$	79.5-80.5	1.8300	1.5588	39.85	38.82
$CH_2Br-CHBr-C\equiv C-C_2H_5$	87-87.5	1.6920	1.5470	44.98	43.44
$CH_2Br-CHBr-C\equiv C-C_3H_7$	100-102	1.6008	1.5348	49.38	48.05
$CH_2Br-CHBr-C\equiv C-C_4H_9$	114-115	1.5191	1.5300	54.50	52.67
$CH_2Br-CHBr-C\equiv C-C_5H_{11}$-iso	121-123	1.4590	1.5238	59.13	57.29
$CH_2=CH-CBr=CBr-CH_3$	57-57.5	1.8304	1.5768	40.89	39.89
$CH_2=CH-CBr=CBr-C_2H_5$	69.5-70	1.7089	1.5640	45.67	44.50
$CH_2=CH-CBr=CBr-C_3H_7$	85.5-86	1.6075	1.5518	50.47	49.12
$CH_2=CH-CBr=CBr-C_4H_9$	101.5-102.5	1.5319	1.5440	55.23	53.74
$CH_2=CH-CBr=CBr-C_5H_{11}$-iso	111-113	1.4614	1.5330	59.88	58.36

Diene dibromides with a conjugated double bond system differ from the acetylene dibromides in a considerably lower boiling point, by higher refractive index, but differ very little in specific gravity. All of these compounds possess high values for molecular refraction and show exaltation. In contrast to acetylene dibromides, the diene dibromides possess quite a pleasant odor. Upon storage they become brownish and polymerize. In an open container, and in small mass, polymerization is in process within a matter of days. Standard inhibitors cut down polymerization. When mixed with alcoholic alkali in the cold, these compounds do not change significantly.

The products of hydrogen bromide rupture from acetylene dibromides are colorless liquids with sharp, persistent odor, characteristic for halogenated acetylene derivatives. Upon storage, and even in the presence of inhibitors, they convert rapidly (after 2-3 days) into a dark-colored resin. Non-reactive with ammoniacal silver oxide solution. Constants are given in Table 2.

It can be seen from Table 2 that for a homologous series there occurs an increase in boiling point according to the rule, and a decrease in specific gravity and refractive index. All of the compounds exhibit considerable molecular exaltation (1.2-1.8).

The authors attempted to obtain the diene tribromide $CH_2=CBr-CBr=CBr-C_2H_5$ by reacting hexenine tetrabromide with alcoholic alkali. The resulting substance boiled over a wide temperature range, and contained a somewhat lower bromine percentage than would be required according to theory. Evidently, the reaction of tetrabromide with alkali proceeds with formation of a mixture of these two substances.

TABLE 2

Substance	Boiling point at 40 mm (in °)	d_4^{20}	n_D^{20}	MR_D	
				Found	Calculated
$CH_2=CBr-C\equiv C-CH_3$	52-53	1.4010	1.5255	31.75	30.59
$CH_2=CBr-C\equiv C-C_2H_5$	67.5-68.5	1.3081	1.5156	36.70	35.20
$CH_2=CBr-C\equiv C-C_3H_7$	83-84	1.2443	1.5092	41.58	39.82
$CH_2=CBr-C\equiv C-C_4H_9$	102-103	1.2005	1.5051	46.24	44.44
$CH_2=CBr-C\equiv C-C_5H_{11}$-iso	113-115	1.1619	1.4998	50.89	49.08

It was thus established that vinylacetylene homologs with a radical in the first position, add bromine predominately at the ethylene bond. The double bond is found to be more reactive, compared to the triple bond. There is no conjugation.

This peculiarity in the addition reaction of vinylacetylene homologs is evidently related to the fact that under the influence of the radicals, electrons of the conjugated system are strongly displaced to the double bond side, and in addition, entrance of bromine into the first position meets with steric hindrance. Of considerable significance is also a decreased tendency for the vinylacetylene system to undergo addition reactions at the 1,4-position, because of peculiarity in their configuration, as was mentioned at the beginning of this article. It is possible that relative stability of the 3,4-product under conditions of the bromine addition reaction is of significance.

EXPERIMENTAL

The vinylalkylacetylenes required for the investigations were prepared according to standard procedures, in yields of 35 to 80% [4]. The yield increased with increase in molecular weight of the alkyl group.

1. Bromination of Vinylalkylacetylenes

Penten-1-ine-3. 53 g (17 ml) of bromine in 100 ml of chloroform was added, over a period of 5 hours, with strong mechanical stirring and cooling to −8° to −10°, to a solution of 43 g of the hydrocarbon (double excess) in 250 ml of chloroform.

After completion of reaction, the chloroform and unreacted hydrocarbon were distilled on a water bath at low pressure, and the residue distilled in vacuo at 10 mm. The chloroform solution of hydrocarbon was again brominated with half the original volume of bromine. The reaction products were separated by the above-indicated method, and the original fraction brominated for a third time. Thus was achieved almost complete utilization of the hydrocarbon, maintaining in twice the amount relative to bromine. About 120 g of bromides was obtained from 100 g of bromine. The fractions resulting from distillation at 10 mm were as follows: 1st, 60-70° 3.8 g; 2nd, 70-79.5° 6.0 g; 3rd, 79.5-80.5° 76 g; 4th, 80.5-100° 2.5 g; 5th, 100-132° 4.4 g; 6th, 132-136° 24.5 g; 7th, 136-145 4.4 g; 8th, residue 5.0 g. With the fractionsdistilling above 100°, there was observed a little decomposition.

Constants for the principal fractions are given in Table 1, analytical data in Table 3. The following frequencies were observed in the combined dispersion spectrum 2347 cm^{-1} (weak), 2240 (very strong), 1612 (indistinct), 1372, 1232, 1157, 1117, 1011 (weak), 711 (average), 669 (very strong). The first two frequencies may belong just to the triple bond. The appearance of 1612 cm^{-1} is related to isomerization of acetylene dibromide into the diene dibromide by exposure to light. Actually, after exposure to light (for 4 hours), the substance upon distillation gives a lower fraction, corresponding to the diene dibromide, and exhibiting a higher refractive index as compared with the original (n_D^{20} 1.5626). The last two frequencies belong to the C−Br bonds.

The main fraction of 5.19 g was ozonized in chloroform.* 1.129 g of ozone was absorbed (for one bond, 1.102 g was required), and ozonization was then terminated. The ozonization rate curve is given in the Figure. After decomposition of the ozonides with 2% H_2O_2, 0.9 g of acetic acid and 2.7 g of acids with b.p. 130-135° at 10 mm were extracted with ether from the solutions. Acetic acid was converted into the anilide, with m.p. 113°, which corresponded with the literature data [5]. Upon cooling, about 1.1 g of α,β-dibromopropionic acid, with m.p. 64-66°, was isolated from the above-boiling acids. A mixture of the substance with known α,β-dibromopropionic acid (prepared by bromination of acrylic acid in chloroform) had the same melting point.

* The authors wish to express their appreciation to A. I. Yakubchik and to N. G. Kasatkina for investigation of the ozonization rate.

0.1024 g sub.: 0.1653 g AgBr. Found %: Br 68.69. $C_5H_4O_2Br_2$. Calculated %: Br 68.77.

7 g of dibromide was oxidized with potassium permanganate (dry permanganate being added in small portions to the vigorously-stirred dibromide mixture, with 100 ml of water and 12 g of $MgSO_4 \cdot 7H_2O$, 11.8 g of permanganate being used). After standard treatment of the reaction mixture, 0.8 g of acetic acid and about 0.8 g of crystalline α,β-dibromopropionic acid, with m.p. 62-64° resulted (after washing the resulting crystals with petroleum ether).

For the 132-136° fraction at 10 mm, there were found: d_4^{20} 2.3496; n_D^{20} 1.6160.

0.1929 g sub.: 0.3623 g AgBr. Found %: Br 79.92. $C_5H_6Br_4$. Calculated %: Br 82.93.

The analytical data indicate that the fraction was the tetrabromide of the original hydrocarbon, which decomposed somewhat upon distillation (with splitting out of hydrogen bromide).

Hexen -1-ine-3. 52 g of bromides was obtained from 20 g of hydrocarbon and 37 g of bromine under the above-indicated conditions.

Fractions resulting from distillation at 10 mm: 1st, 70-80° 2 g; 2nd, 80-85° 1.8 g; 3rd, 85-90° 21.8 g; 4th, 90-95° 2 g; 5th, 95-100° 1.5 g; 6th, 100-140° 2 g; 7th, 140-150° 10 g; 8th, residue 4.6 g.

Constants for the major fractions are given in Table 1, the analytical data in Table 3. First fraction had n_D^{20} 1.5544.

6 g of the substance was ozonized. After standard treatment of the ozonide, 1.2 g of propionic acid and 3.5 g of acids distilling in the range 125-135° at 10 mm resulted. The propionic acid was identified as the anilide with m.p. 104°. Crystalline α,β-dibromopropionic acid (m.p. 62-64°) was isolated from the higher fraction.

The sixth fraction was the tetrabromide of the initial hydrocarbon which decomposed somewhat during the distillation. For it there were found: d_4^{20} 2.2035; n_D^{20} 1.6020.

0.1476 g sub.: 0.2728 g AgBr. Found %: Br 78.65. $C_6H_8Br_4$. Calculated %: Br 79.96.

Hepten -1-ine-3. 105 g of bromides resulted from 42 g of hydrocarbon and 71 g of bromine. The substance was separated into the following fractions as the result of distillation: 1st, to 94° 3.4 g; 2nd, 94-99° 3.6 g; 3rd, 99-104° 60.1 g; 4th, 104-110° 6.0 g; 5th, residue 27 g. In this case, and in subsequent cases, constants for the principal fractions are given in Table 1, analytical data in Table 3.

Octen -2-ine-3. 109 g of bromides resulted from 54 g of hydrocarbon and 70 g of bromine. Distillation at 10 mm gave the following fractions: 1st, 107-110° 1.8 g; 2nd, 110-116° 67 g; 3rd, 116-122° 4.2 g; 4th, residue 32.8 g.

7-Methyloctcn —1-ine-3. 85 g of bromides resulted from 45 g of hydrocarbon and 53 g of bromine. Distillation at 10 mm yielded the following fractions: 1st, 117-122° 1.5 g; 2nd, 122-126° 45.5 g; 3rd, 126-130° 4.5 g; 4th, residue 28 g.

2. Isomerization of Acetylene Dibromides into Diene Bromides

0.1 mole of acetylene dibromide was dissolved in 50 ml of ether and heated under reflux on a water bath with 50 ml of 48% hydrobromic acid and 10 g of Cu_2Br_2 for 4-6 hours. The mixture was then diluted with water, the ether layer separated, and the residue extracted with ether. The ether solutions of dibromide were washed with water, dried with $CaCl_2$ and distilled: ether was distilled off at normal pressure, the residue distilled in vacuo. Here the main fraction went over within a range of 0.5-1°, the yield of this fraction constituting about 70-80% of the total material. Constants for the diene dibromides are given in Table 2, and the analytical data in Table 3.

The relationship between diene dibromides and alcoholic alkali was studied under the following conditions: a weighed sample (about 1 g) was added in the cold to 15% ethanolic solution of KOH, and after a lapse of 4-5 hours the amount of bromide ion determined in the solution. The first member of the diene dibromide series in this case lost 5% bromine, and the second 6%.

The following frequencies were found in the combined dispersion spectrum: 143, 172, 214 (weak), 460, 510, 917, 956 (average), 1160 (strong), 1257, 1295, 1403 (average), 1517 (weak), 1611 (very strong), 2932, 2977, 3029 (weak) cm^{-1}. *

* The authors wish to express their appreciation to T. V. Yakovleva for assistance in measuring the spectra.

TABLE 3

Substance	Sample weight (in g)	AgBr (in g)	% Br	
			Found	Calculated
$CH_2Br-CHBr-C\equiv C-CH_3$	0.1576	0.2595	70.08	70.74
$CH_2Br-CHBr-C\equiv C-C_2H_5$	0.1356	0.2120	62.52	66.61
$CH_2Br-CHBr-C\equiv C-C_3H_7$	0.1393	0.2026	63.11	62.93
$CH_2Br-CHBr-C\equiv C-C_4H_9$	0.1572	0.2168	58.68	59.64
$CH_2Br-CHBr-C\equiv C-C_5H_{11}$-iso	0.1769	0.2365	56.89	56.67
$CH_2=CH-CBr=CBr-CH_3$	0.1900	0.3130	70.09	70.74
$CH_2=CH-CBr=CBr-C_2H_5$	0.1908	0.2962	66.06	66.61
$CH_2=CH-CBr=CBr-C_3H_7$	0.1760	0.2604	62.96	62.93
$CH_2=CH-CBr=CBr-C_4H_9$	0.1186	0.1650	59.20	59.64
$CH_2=CH-CBr=CBr-C_5H_{11}$-iso	0.1083	0.1440	56.58	56.67
$CH_2=CBr-C\equiv C-CH_3$	0.1348	0.1744	55.05	55.11
$CH_2=CBr-C\equiv C-C_2H_5$	0.1532	0.1804	50.10	50.25
$CH_2=CBr-C\equiv C-C_3H_7$	0.1218	0.1312	45.83	46.18
$CH_2=CBr-C\equiv C-C_4H_9$	0.1347	0.1352	42.71	42.71
$CH_2=CBr-C\equiv C-C_5H_{11}$-iso	0.1482	0.1373	39.40	39.74

3. Synthesis of Monobromovinylacetylenes

Upon treating acetylene dibromides in the cold with a slight excess of 15% alcoholic KOH, exactly one-half of the bromine contained in the compound is split off in the form of bromide ion Thus, a 7.2 g batch of the first homolog lost in this case 2.55 g of bromine in the form of bromide ion, which constituted 50.06% (7.2 g), and of the second homologs 2.36 g of bromine, which constituted 49.2%, analogous data for the third and fourth homologs being 48.8 and 48.0%.

After dilution of the reaction mixture with water, the reaction products were distilled with steam. Yield of bromovinylacetylene amounted to 55-60%. Their constants are given in Table 2, the analytical data in Table 3.

4. Reaction of Alcoholic Alkali With Hexenine Tetrabromide

2.2 g of KOH in alcoholic 10% solution was added to 12.8 g of tetrabromide, with stirring and cooling. Potassium bromide precipitated immediately. An oil separated from the reaction mixture upon dilution with water, which, after washing with water, and drying over $CaCl_2$, was distilled in vacuo at 10 mm. The following fractions resulted: 1st, to 116° 2 g; 2nd, 116-121° 4.2 g; 3rd, above 121° 2 g.

For the 116-121° fraction at 10 mm: d_4^{20} 1.9744; n_D^{20} 1.5935.

0.1520, 0.1762 g sub.: 0.2627, 0.3028 g AgBr. Found %: Br 73.55, 73.13. $C_6H_7Br_3$. Calculated %: Br 75.19.

SUMMARY

1. The sequence of bromine addition to vinylalkylacetylenes has been investigated. It has been established that, in contrast to vinylacetylene, homologs of the indicated type add bromine chiefly at the double bond. The structure of the reaction products has been proved by ozonization and by oxidation, as the result of which there are formed α,β-dibromopropionic acid and the corresponding unsubstituted carboxylic acids.

2. Upon reacting Cu_2Br_2 with acetylenic dibromides, there have been obtained diene dibromides which differ considerably, by lower boiling points, stability to alkali, and tendency to polymerize.

3. A series of monobromovinylacetylenes has resulted from reaction of acetylene dibromides with alcoholic alkali.

4. Peculiarities of reaction for vinylacetylene homologs relative to bromine have been explained on the assumption of molecular rearrangement of these substances under the influence of a reactive radical center on one side of the double bond, as well as conditions of steric hindrance to the addition reaction.

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* See Consultants Bureau Translation, page 745.

REACTION OF PHOSPHORUS TRICHLORIDE AND OF TRIBROMIDE WITH DIMETHYLCYCLOPROPYLCARBINOL

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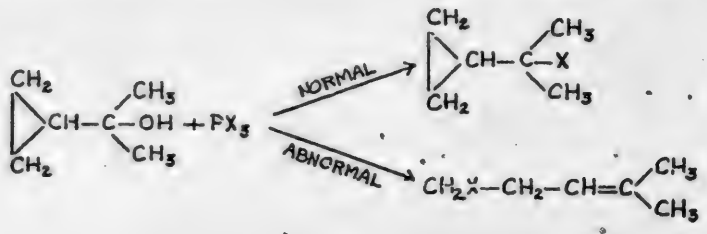
It was demonstrated in the works by one of us [1, 2] that interaction of methylcyclopropylcarbinol with phosphorus halides proceeds "abnormally", as the result of which there are formed unsaturated halogen derivatives with an open chain of carbon atoms. It has been established that the degree to which a three-membered ring is opened up depends upon the nature of the halogen atom. If iodine causes complete opening of the ring [3], then bromine does not open it completely (70%) and chlorine causes opening only on a small scale (10%) [1]. The introduction of two chlorine atoms into the *a*-position of a three-membered ring leads to formation of an "abnormal" reaction product to the same degree as does one bromine atom (70%).

It was of interest to study the interaction of dimethylcyclopropylcarbinol with PCl_3 and PBr_3.



Considering the tertiary character of carbinol, ring opening on a larger scale than in the case of methylcyclopropylcarbinol might be expected.

Bruylants [4], by reacting dimethylcyclopropylcarbinol with hydrogen bromide, obtained a bromide to which he attributed the cyclic structure. Upon splitting out hydrogen bromide, there resulted a hydrocarbon which was accepted by the authors as isopropenylcyclopropane; however, from its properties, this hydrocarbon was found to be identical with 2-methylpentadiene-2,4. It should be considered that the bromide obtained by Bruylants also possessed an open chain of carbon atoms.

In a study of the reaction of hydrogen chloride with the same carbinol, Bruylants prepared the chloride, to which he at first also attributed the cyclic structure. Later, the structure, 5-chloro-2-methylpentane-2, was attributed to this chloride [5].

T. A. Favorskaya [6-9], who studied in detail the properties and the conversion of tertiary alcohols of the cyclopropane series, proved that upon interacting dimethylcyclopropylcarbinol with hydrochloric acid there is indeed formed an unsaturated primary monochloride with an open chain of carbon atoms. A dichloride was formed as a secondary product.

In the present investigation, interaction of dimethylcyclopropylcarbinol with PCl_3 and PBr_3 has been studied.

After fractionation of the interaction products of carbinol with PCl_3, the chloride was isolated in yield 45% of theory. In addition, a hydrocarbon was obtained, which resulted from spontaneous splitting out of hydrogen chloride.

In its properties the chloride hardly differed from chlorides that were obtained by Bruylants and Favorskaya by reacting carbinol with hydrochloric acid.

Frequencies of 655 and 718 cm^{-1} in the combined dispersion spectrum of the chlorides indicated presence of a chlorine atom on a primary carbon, and the intense line with a frequency of 1673 cm^{-1}, presence of the group $-HC=C\langle^{R}_{R}$. There are group frequencies in the spectrum which definitely indicated the presence of chloride addition which contained a tri-membered ring (877, 924, 1193 cm^{-1}).

With ozonolysis of the chloride, acetone, acetone peroxide and β-chloropropionic acid were isolated. This confirmed that the chief component part of the chloride was 5-chloro-2-methylpentene-2.

The hydrocarbon which was isolated by distillation of the crude chloride was found, from its properties, to be identical with isopropenylcyclopropane.

Intense lines with frequencies 895, 968, 1191, 3011, 3081 cm^{-1} were found in the combined dispersion spectrum for this hydrocarbon, which characterized the cyclopropane structure, and a line at the 1648 cm^{-1} frequency, characterizing the group $-C(=CH_2)-R$.

Upon hydrogenation over platinum catalyst, the quantity of hydrogen absorbed corresponded to one double bond.

Thus, upon interacting dimethylcyclopropylcarbinol with PCl_3, both the normal and the abnormal reactions proceeded on the same scale.

By splitting out of hydrogen chloride from 5-chloro-2-methylpentene-2, by reacting with KOH, a diene hydrocarbon resulted, which upon hydrogenation added 2 moles of water. The combined dispersion spectrum for this hydrocarbon, and its properties, corresponded to 2-methylpentadiene-2,4.

Upon reacting dimethylcyclopropylcarbinol with PBr_3, there resulted the bromide in yield of 86% of theory. The hydrocarbon was not found among the reaction products.

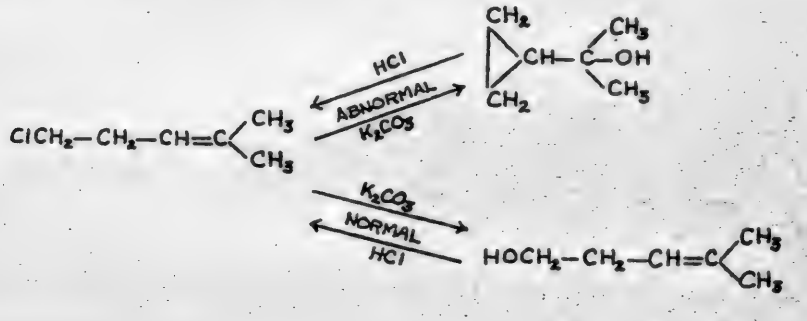
In the combined dispersion spectrum for bromide, frequencies of 563 and 643 cm^{-1} indicated presence of bromine at a primary carbon. The 1672 cm^{-1} frequency indicated presence of the grouping $-HC=C(R)R$. Frequencies which characterize a three-membered ring were not present in the spectrum.

Upon rupture of hydrogen bromide from the resulting bromide by reacting it with KOH, a hydrocarbon was prepared which was found to be 2-methylpentadiene-2,4.

Thus, the interaction of dimethylcyclopropylcarbinol with PBr_3 leads to formation of the abnormal product only – 5-bromo-2-methylpentene-2.

The works of Bruylants [5] and Favorskaya [7] have established that 5-chloro-2-methylpentene-2 upon saponification with potash converts into dimethylcyclopropylcarbinol. According to Favorskaya's directions, the reaction products contain as impurity an unsaturated compound which does not possess chlorine.

The authors effected saponification of chloride under the conditions given in Favorskaya's work. In the combined dispersion spectrum for the saponification products, all of the frequencies for dimethylcyclopropylcarbinol were found. Along with this fact, there were preserved in the spectrum markedly weakened lines of the initial chloride. Determination of chlorine content indicated that the saponification products contained about 18% of unchanged chloride. Moreover there was found in the spectrum a line of frequency 1674 cm^{-1}, the intensity of which was considerably greater than could be expected from the unsaturated chloride content. This data makes it possible to assume that upon saponification of unsaturated chloride, there is formed, along with the tertiary cyclic carbinol, 2-methylpentene-2-ol-5 – the normal product of chloride saponification.



EXPERIMENTAL

Dimethylcyclopropylcarbinol

The initial acetylcyclopropane was prepared according to the method of Wagner [10] as modified by Slobodin and Shokhor [11].

Dimethylcyclopropylcarbinol was prepared, according to the standard method, from acetylcyclopropane and methyl magnesium iodide. Yield of carbinol was 75% of theory. The carbinol boiled at 122-123°; d_4^{20} 0.8816; n_D^{20} 1.4338; MR_D 29.53. $C_6H_{12}O$. Calculated MR_D 29.94.

Combined dispersion spectrum:

262 (0.5), 278 (0.5), 333 (6), 355 (3), 368 (0.5), 389 (0.5), 405 (0.5), 441 (0.5), 478 (2), 514 (3), 539 (3), 588 (2), 632 (2), 691 (15), 742 (1), 786 (4), 822 (7), 844 (9), 851 (9), 913 (9), 933 (9), 958 (9), 997 (1), 1023 (0.5), 1064 (4w), 1105 (1), 1141 (4), 1172 (4), 1201 (20), 1238 (3), 1364 (2), 1424 (9), 1442 (9), 1467 (9), 2867 (2), 2911 (9), 2930 (9), 2971 (10), 3008 (15), 3073 (4w).

I. Reaction of PCl_3 With Dimethylcyclopropylcarbinol

A few drops of pyridine was added to 20 g of PCl_3 dissolved in 150 ml of dry ether. 40 g of carbinol and 16 g of pyridine as a mixture was added to the mixture gradually through a dropping funnel. The rate of addition was regulated in such a manner that the temperature of the mixture did not exceed 30-35°. After addition of a small amount of the carbinol, the mixture was kept for 0.5 hour at room temperature, after which it was poured into ice water The ether solution was separated, and the aqueous layer extracted with ether. The combined ether solution was dried over calcium chloride. After distilling off the ether, hydrogen chloride evolution was observed.

Isolation of the fractions: 1st, 54-78°, 8 g (hydrocarbon); 2nd, 79-128°, 7 g; 3rd, 129-133°, 20.5 g (chloride).

Upon second distillation, the chloride distilled over at 132-134°; d_4^{20} 0.9164; n_D^{20} 1.4468; MR_D 34.54.

Found %: Cl 31.00. $C_6H_{11}Cl$. Calculated %: Cl 29.96; MR_D 34.32.

Combined dispersion spectrum for the chloride:

261 (6), 375 (0.5), 461 (2), 512 (0.5), 590 (0.5), 655 (10), 718 (10), 751 (8), 777 (0.5), 799 (5), 834 (5), 877 (0.5), 924 (1), 971 (1), 1029 (4), 1070 (3), 1103 (3), 1146 (2), 1193 (1), 1234 (2), 1278 (2), 1316 (4), 1351 (3), 1381 (10), 1445 (10), 1673 (20), 2856 (2), 2911 (5), 2959 (3), 2997 (0.5).

Ozonolysis of the Chloride. 4.2 g of chloride was dissolved in ethyl chloride and ozonized with 3% ozone. The ozonide, after removal of solvent, was decomposed by boiling with water. On cooling, acetone peroxide crystals, m.p. 129°, separated on the walls of the flask. Upon heating on a spatula they exploded. The aqueous solution was distilled. Acetone was found in the fraction boiling up to 100°, according to reaction with 2,4-dinitrophenylhydrazine. The residue in the distilling flask was extracted with ether. After removal of the ether, β-chloropropionic acid with m.p. 38° was isolated.

Saponification of the Chloride. 4 g of the chloride was boiled for 12 hours in a flask equipped with reflux condenser, with 50 ml of 10% potash solution. The reaction products were extracted with ether. The ether solution was dried overnight over sodium sulfate. Upon fractionation, the fraction with m.p. 122-124° was isolated in the amount of 3.2 g; n_D^{20} 1.4341 (dimethylcyclopropylcarbinol n_D^{20} 1.4338).

0.1474, 0.1980 g sub.: 0.0340, 0.0407 g AgCl. Found %: Cl 5.1, 5.7, which, recalculated on the chloride content, amounted to about 18%.

Combined dispersion spectrum:

251(1), 278 (1), 333 (2), 392 (0.5), 417 (0.5), 518 (1), 538 (1), 655 (1), 692 (10), 720 (2), 750 (1), 786 (3), 823 (4), 847 (7w), 912 (4), 931 (6), 1000 (0.5), 1013 (1), 1065 (2w), 1106 (1), 1142 (2), 1199 (15), 1238 (2), 1384 (3w), 1448 (8w), 1674 (4), 2850 (4), 2875 (4), 2916 (4), 2937 (4), 2972 (6), 3010 (8), 3078 (3).

HCl Rupture from the Chloride. 13.5 g of chloride was gradually added from a dropping funnel to 7 g of KOH in 60 ml of the monoethyl ester of ethylene glycol which was heated to boiling. The hydrocarbon which formed was passed without condensation through a reflux condenser in which hot water circulated. The vapors were then condensed in a coil and collected in a receiver. Yield of hydrocarbon was 6.5 g (70%). Upon distillation, the hydrocarbon went over at 76.5-77°; n_D^{20} 1.4518. Upon prolonged storage the hydrocarbon polymerized completely.

Combined dispersion spectrum of the hydrocarbon:

254 (0.5), 361 (7), 437 (7), 523 (6), 811 (5), 860 (0.5), 899 (6), 1067 (1), 1144 (7), 1215 (10), 1290 (6), 1332 (6), 1380 (5), 1420 (0.5), 1453 (7), 1546 (0.5), 1559 (0.5), 1600 (9), 1623 (0.5), 1655 (15w).

The hydrocarbon reacted readily with maleic anhydride to form the polymer product, which is in agreement with the literature data [12].

0.6091 g of hydrocarbon was hydrogenated in the presence of platinum catalyst in alcoholic solution. Hydrogen used was 344 ml (0°, 760 mm), which corresponded to an excess of 3.4%, as against that calculated for the double bonds.

Hydrocarbon from the 54-78° Fraction. The hydrocarbon was distilled three times over metallic sodium. A hydrocarbon of b.p. 70-72° was isolated.

d_4^{20} 0.7514; n_D^{20} 1.4260; MR_D 27.96. C_6H_{10} . Calculated: MR_D 27.95 (the increment for a three-membered ring was adopted as equal to 0.7).

Combined dispersion spectrum:

229 (0.5), 265 (5 w), 392 (2), 412 (4), 475 (8), 482 (0.5), 530 (2), 696 (0.5), 713 (6), 729 (2), 818 (3), 895 (8 w), 968 (6), 992 (2), 1021 (3), 1094 (2 w), 1142 (1), 1191 (10), 1238 (1w), 1291 (2 i), 1331 (0.5), 1390 (5w), 1428 (5), 1458 (5), 1637 (10), 1648 (8), 2916 (3), 2989 (1), 3011 (8), 3081 (4w).

For determination of conjugated diene, the hydrocarbon was sealed in an ampoule with a titrated solution of maleic anhydride; the mixture was heated 4 hours on a boiling water bath. Unreacted maleic anhydride was extracted with hot water and titrated with alkali. The difference between maleic anhydride in the initial solution and in the solution after heating with the hydrocarbon made it possible to calculate the content of conjugated diene, which was found to be equal to 3%.

0.3830 g of hydrocarbon was hydrogenated in the presence of platinum catalyst in alcoholic solution. 110 ml of hydrogen was used for the hydrogenation (0°, 760 mm) which corresponded to an excess of 5%, calculating on one double bond basis.

II. Reaction of PBr_3 with Dimethylcyclopropylcarbinol

20 g of carbinol was added to 60 g of PBr_3 under the conditions described above for synthesis of the chloride. Yield of bromide was 86% of theory. Upon fractionation, almost no hydrogen was obtained. The bromide, which was dried over calcium chloride, boiled at 154-155°; d_4^{20} 1.2506, n_D^{20} 1.4780; MR_D 36.84. $C_6H_{11}Br$. Calculated: MR_D 37.18.

Analysis for bromine content gave somewhat high results.

Combined dispersion spectrum for bromide:

214 (6), 263 (1), 299 (0.5), 457 (3), 510 (0.5), 563 (8), 643 (10), 744 (2), 795 (2), 836 (1), 1205 (2), 1271 (2), 1313 (2), 1349 (2), 1382 (6), 1441 (5), 1618 (1), 1645 (1), 1672 (10), 2862 (3), 2914 (6), 2967 (4).

HBr Rupture from Bromide. Rupture was carried out under conditions described above for the chloride. 20 g of the bromide and 7.5 g of KOH as a solution in 80 ml of the monoethyl ester of ethylene glycol were taken. The resulting hydrocarbon boiled at 76-77°; n_D^{20} 1.4530. Upon prolonged storage the hydrocarbon polymerized completely.

The combined dispersion spectrum for the hydrocarbon was identical to the spectrum of the hydrocarbon which resulted from the chloride.

SUMMARY

1. By reaction of PCl_3 with dimethylcyclopropylcarbinol, there is formed up to 50% of an abnormal reaction product —5-chloro-2-methylpentene-2. Formation of isopropenylcyclopropane is observed at the same time.

2. Upon reacting PBr_3 with dimethylcyclopropylcarbinol, only the abnormal reaction product —5-bromo-2-methyl-pentene-2— is formed.

3. The Bruylants and Favorskaya observations on conversion of 5-chloro-2-methyl-pentene-2 by saponification to dimethylcyclopropylcarbinol, have been spectroscopically confirmed. The data obtained also make it possible to assume that in addition to the above, there is also formed an unsaturated alcohol, of open carbon chain, upon saponification.

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* See Consultants Bureau Translation, page 243.
** See Consultants Bureau Translation, page 259.
*** See Consultants Bureau Translation, page 613.
**** See Consultants Bureau Translation, page 2225.

THE CONVERSION MECHANISM OF TERTIARY ALCOHOLS OF THE CYCLOPROPANE SERIES UNDER THE INFLUENCE OF MINERAL AND ORGANIC ACIDS

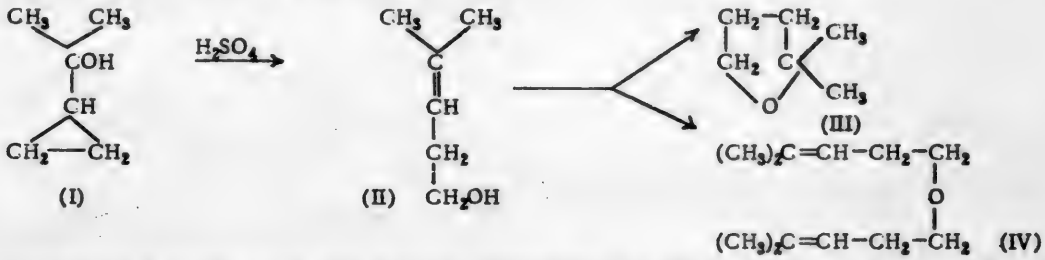
III. THE INTERACTION OF DIMETHYLCYCLOPROPYLCARBINOL, METHYLETHYLCYCLOPROPYLCARBINOL AND METHYLISOPROPYLCYCLOPROPYLCARBINOL WITH SULFURIC ACID

T. A. Favorskaya, N. V. Shcherbinskaya and E. S. Golovacheva

All of the known literature investigations on interaction of tertiary alcohols of the cyclopropane series with sulfuric acid have been carried out for the purpose of synthesizing and studying various hydrocarbons. To such belong those of Keersblick [1], Volkenburgh [2] and Slabey [3]; all of these authors used concentrated sulfuric acid, and therefore no other products were obtained than the dehydration products. In studying the interaction of dilute sulfuric acid with methylphenyl- and diphenylallyl-carbinols, the authors, with Sh. A. Fridman [4], established that these alcohols are ruptured, with simultaneous formation of acetophenone and benzophenone. Upon reacting methylphenylcyclopropylcarbinol with dilute sulfuric acid, there was observed, in addition to the formation of unsaturated hydrocarbon, and enlargement of the three-membered cycle into a four-membered, with formation of methylphenylcyclobutanol [5]. On the other hand, upon heating dimethyl- and methylethylcyclopropylcarbinols with dilute formic acid [6, 7], the authors succeeded in synthesizing a whole series of products, and in determining that the first substances formed during the reaction are the unsaturated primary alcohols of 2-methy-penten -2-ol-5 (II) and 3-methylhexen -3-ol-6 (VII), which then become cyclized into derivatives of tetrahydrofuran, and convert into a series of other compounds as well.

Because of a desire to determine by which of the above-described mechanisms interaction of aliphatic alcohols of the cyclopropane series takes place with sulfuric acid, the authors carried this reaction out with acid of varying concentration (1: 4, 1: 5 and 1: 10).

With dimethylcyclopropylcarbinol (I), the first reaction product in all experiments carried out was found to be the primary alcohol (II), which then, on the one hand, isomerized into 2,2-dimethyltetrahydrofuran (III), and on the other — to form a small amount of ether (IV):

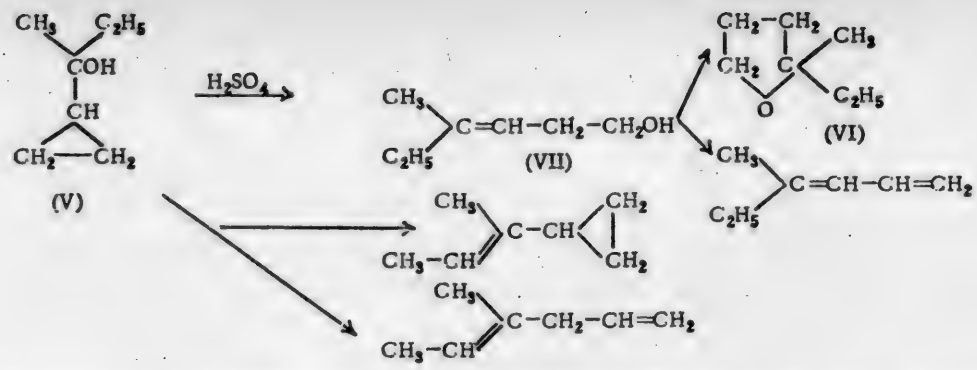


Dehydration of alcohol (I) to form the cyclic hydrocarbon, as used with concentrated sulfuric acid in the authors' experiments, was not observed. It was demonstrated that the concentration of acid affects considerably the yields of various reaction products: the lower the acid concentration the higher the yield of products (II) and (III) and the less of ester (IV) as well as resinous polymerization products.

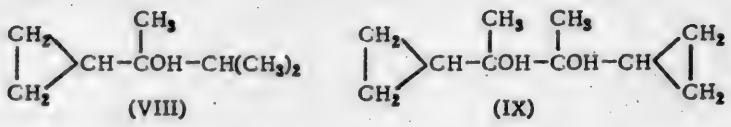
Reaction of Methylethylcyclopropylcarbinol (V). This was carried out only with sulfuric acid at a dilution of 1:5, since it was possible at this concentration to obtain all of the reaction products The authors isolated in this case a mixture of hydrocarbons which, according to the constants, corresponded to that resulting from the reaction of methylethylcyclopropylcarbinol [7] and formic acid: 2,2-methylethyltetrahydrofuran (VI), a primary alcohol — 3-methylhexen -3-ol-6 (VII), and a number of polymeric products. (See diagram at top of next page).

It was not possible in this instance to isolate a simple ether corresponding to alcohol (V).

The next alcohol investigated was methylisopropylcyclopropylcarbinol, prepared by reacting magnesium



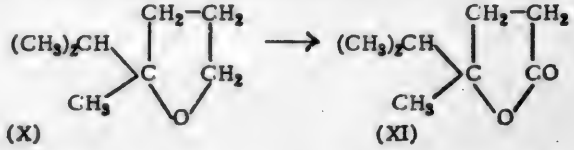
isopropylbromide with acetyltrimethylene. There were obtained as the result of this reaction, in addition to alcohol (VIII), the glycol-2,3-dicyclopropylbutandiol-2,3 (XI).



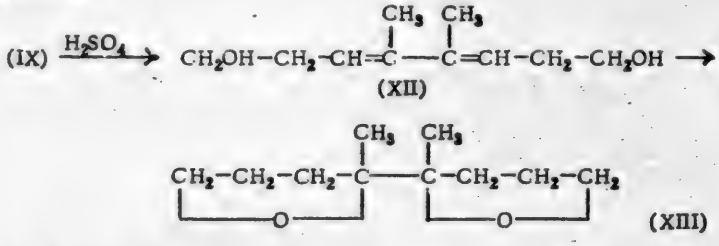
Slabey [3], who obtained methylisopropylcyclopropylcarbinol by the same procedure on a very small scale makes no reference to formation of this glycol. A small amount of this glycol was obtained by one of us [8]; however, it was not possible to carry out a more detailed investigation. The glycol was oxidized with lead tetraacetate according to the method of Criege [9], from which there resulted a single reaction product – acetyltrimethylene.

Both the alcohol and the glycol were reacted with dilute sulfuric acid (1: 10). In the case of the alcohol, the authors obtained 2,2-methylisopropyltetrahydrofuran; it was not possible to isolate the corresponding primary alcohol because of the small volume of alcohol (VIII) at the authors' disposal. Nevertheless, the authors consider it allowable in this case again to accept the same reaction mechanism as was applied to the first two alcohols investigated [6, 7].

The structure for 2,2-methylisopropyltetrahydrofuran (X), was proved by its oxidation with $KMnO_4$ solution, whereby the lactone of γ δ,dimethyl-γ-hydroxy-caproic acid (XI) resulted:

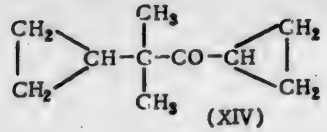


Upon reacting the glycol with sulfuric acid, one might expect formation of the ditetrahydrofuran derivative (XIII), according to the scheme:



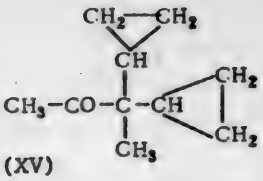
On the other hand, however, since glycol (IX) is a pinacol, then one might expect a pinacolic rearrangement, with formation of two possible pinacolines (XIV) and (XV): (See top of next page).

Experiments demonstrated that the reaction proceeds along both possible directions. A small amount of ketone was isolated from the reaction products, the composition of which corresponded to the formula $C_{10}H_{16}O$.



(XIV)

or



(XV)

The amount did not permit the authors to determine which of the two ketones resulted at the time. The main direction was apparently conversion of glycol into the unsaturated diprimary glycol (XII), but the presence of a conjugated double bond system in it caused immediate polymerization of the substance when a certain specific temperature was reached. The amount of glycol distilled was so small that it was possible only to determine the refractive index and the number of active hydrogen atoms, and to ascertain the presence of double bonds on the basis of rapid decolorization of $KMnO_4$ solution. All of these data indicated that, in all probability, reaction of pinacol with sulfuric acid was halted at the first stage of 1,3-diene glycol formation; however, cyclization of the latter to tetrahydrofuran did not occur.

EXPERIMENTAL

Dimethylcyclopropylcarbinol (I)

N. V. Shcherbinskaya

The carbinol was prepared from methyl magnesium bromide and acetyltrimethylene. The resulting crude alcohol was purified by oxidation ($KMnO_4$ solution). The yield of alcohol with b.p. 120 - 123° was 54 - 55% of theory.

Interaction of Dimethylcyclopropylcarbinol With Sulfuric Acid

In the three experiments carried out, acid of various concentrations was used, and at the same time the interaction period was decreased. Experiments carried out can be summarized in the following Table:

Reaction product	H_2SO_4 (1: 4) 2 hours (in %)	H_2SO_4 (1: 5) 2 hours (in %)	H_2SO_4 (1: 10) 1 hour (in %)
Dimethyltetrahydrofuran	31.1	44.1	51.6
2-Methylpenten-2-ol-5	–	1	5.0
2-Methylpenten-2-ol-5 ether	13.5	10.0	–
Resinous residue (polymerization product)	8.0	7.5	Small amount

Experiment I. 30 g of alcohol was boiled for 2.5 hours with 125 ml of H_2SO_4 (1: 4). The reaction products were extracted with ether and washed with soda solution. The following fractions resulted upon distillation. 1st: 90 - 92°, 9.4 g; 2nd: 103 - 105° at 13 mm, 3.7 g and the resinous residue was 2 g.

Experiment II. 68 g of alcohol was boiled for 2 hours with 240 ml of H_2SO_4 (1: 5). After similar treatment and distillation the following fractions were isolated: 1st: 90 - 92°, 30 g; 2nd: 61 - 63° at 11 mm, 0.65 g; 3rd: 101 - 103° at 10 mm, 6.2 g; 4th: weight of resin was 4.2 g.

Experiment III. 40 g of alcohol was boiled for 1 hour with 220 ml of H_2SO_4 (1: 10). The following fractions were obtained after similar treatment: 1st: 90 - 92°, 20.65 g, 2nd: 61 - 63° at 11 mm, 2.0 g. There remained in the flask only a very negligible amount of resin.

Furthermore, in all three experiments there resulted fractions with b.p. 92 - 110° – a mixture of tetrahydrofuran and acetyltrimethylene – which gave a 2,4-dinitrophenylhydrazone precipitate with m.p. 145 - 146°. The pure acetyltrimethylene was not isolated from these fractions because of its small volume. As was indicated above [6], the acetyltrimethylene is usually present in small amount with the dimethylcyclopropylcarbinol.

The fraction with b.p. 61 - 63° at 11 mm corresponded to the primary alcohol (II):

d_4^{20} 0.8573; n_D^{20} 1.4460; MR_D 30.74. $C_6H_{12}O$. Calculated: MR_D 31.20.

0.1332 g substance: 31 ml CH_4 (21°, 756.8 mm).

The fraction with b.p. 101 - 103° at 10 mm (115 - 116° at 25 mm) gave negative test for hydroxyl and carbonyl groups: on the basis of the analytical data for this fraction, the formula which should be attributed to it is that of a simple ether (VI).

d_4^{20} 0.8416; d_4^0 0.8570; n_D^{20} 1.4530; MR_D 58.06. $C_{12}H_{22}O_2$. Calculated: MR_D 58.32.
0.1192 g substance: 0.3452 g CO_2; 0.1272 g H_2O. 0.1213 g substance; 14.23 g benzene: Δt 0.24°.
Found %: C 78.97; H 11.94; M 182.2. $C_{12}H_{22}O$. Calculated %: C 79.05; H 12.16; M 182.0.

The ether rapidly decolorized $KMnO_4$ solution, and gave acetone upon oxidation, which was characterized through its 2,4-dinitrophenylhydrazone, with an m.p. of 125 - 126°, after double recrystallization from alcohol. A mixed sample did not give depression. It was not possible to isolate any other oxidation products. The resinous residue in the distilling flask was evidently the hydrocarbon polymerization product, which can be formed by dehydration of the primary alcohol (II).

Methylethylcyclopropylcarbinol (V)

The alcohol was prepared from ethyl magnesium bromide and acetyltrimethylene. The resulting product, with b.p. 138 - 144°, was purified by oxidation with $KMnO_4$ solution to remove unsaturated additives. The yield of pure alcohol, with b.p. 141 - 143°, was 54% of theory.

Interaction of Methylethylcyclopropylcarbinol With Sulfuric Acid

50 g of methylethylcyclopropylcarbinol was boiled for 2 hours with 120 ml of H_2SO_4 (1:5). The reaction products were extracted with ether, the extracts washed with soda solution. After drying and distilling off the solvent, the products were distilled at first under atmospheric pressure. The following fractions resulted from repeated fractionations: 1st 100 - 107°, 12.5 g (29%), 2nd 107 - 112°, 2g (~5.5%), 3rd 119 - 121°, 12.0 g (24%). The residue was fractionated in vacuo, whereupon there resulted 0.5 g of substance with b.p. 69 - 71° at 11 mm. There also remained in the flask 1.5 g of resin.

The fraction with b.p. 100 - 107° was a mixture of hydrocarbons. Its purification from traces of acetyltrimethylene was carried out by means of heating with metallic Na. A substance resulted with boiling point 100 - 106°, d_4^{20} 0.7852, n_D^{20} 1.4425. The constants obtained were very close to the constants for the hydrocarbon mixture isolated from reaction products of methylethylcyclopropylcarbinol with formic acid [7].

The fraction with b p. 107 - 112° was found to be acetyltrimethylene; from it resulted the 2,4-dinitrophenylhydrazone with m p 145° (from alcohol).

The fraction with b.p. 119 - 121°, n_D^{20} 1.4228, was found to be 2,2-methylethyltetrahydrofuran

The substance with b.p. 69 - 71° at 11 mm, n_D^{20} 1.4500, corresponded to the primary alcohol — 3-methylhexen -3-ol-6.

0.0998 g substance: 21 ml CH_4 (15°, 758.5 mm). Yield OH No. 0.997. $C_7H_{14}O$. Calculated OH No. 1.

Methylisopropylcyclopropylcarbinol (VIII)

E. S. Golovacheva

62 g (0.5 mole) of isopropyl bromide was added to 12 g of magnesium covered with ether. After termination of the addition, the reaction mixture was stirred for 2 hours, after which the acetyltrimethylene was added in an equal volume of ether in the amount of 32 g (3/4 of the theoretical amount, since a portion of the magnesium did not enter into reaction). The reaction mixture was further stirred and heated for 1 hour and left overnight. The reaction products, after decomposition of the organo-magnesium complex with water and dilute H_2SO_4, were extracted with ether and the extract washed with soda solution and dried with potash. After distilling off the ether, and distilling at 3 mm, 2 substances were isolated: 1) with a b.p. of 45 - 46°, 13 g (26.6%), and 2) with a b.p. of 128 - 130°, 2 g (6.17%). The second substance crystallized in the receiver.

Investigation of the substance with b.p. 45 - 46° at 3 mm. It boiled at 61.5 - 62° at 17 mm, 75 - 78° at 38 mm.

n_D^{20} 1.4465; d_4^{20} 0.8888; MR_D 38.47; $C_8H_{16}O$. Calculated MR_D 39.13. Slabey data for methylisopropylcyclopropylcarbinol [3].

n_D^{20} 1.4465; d_4^{20} 0.8856; MR_D 38.63.
0.0752 g substance: 0.2063 g CO_2; 0.0840 g H_2O. 0.1016 g substance: 19.8 ml CH_4 (13°, 752.8 mm).
Found %: C 74.85; H 12.49; number of active hydrogens 0.99. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50; number of active hydrogens 1.0.

Investigation of the substance with b.p. 128 - 130° at 3 mm. The crystals pressed out on a porous plate melted at 71 - 72°.

Recrystallization from alcohol did not increase the melting point.

0.0911 g substance: 0.2359 g CO_2; 0.0865 g H_2O; 0.1198 g substance; 11.1 g benzene: Δt 0.256°. Found %: C 70.62; H 10.60; M 213. $C_{10}H_{18}O_2$. Calculated %: C 70.59. H 10.59; M 170.

Oxidation of the Glycol with Lead Tetraacetate. 1 g of the glycol and 5 g of freshly-prepared lead tetraacetate (an excess) were heated on a water bath at 50 - 60° for 2 hours. After cooling, the flask contents were neutralized with soda, the precipitated salts filtered off, the filtrate distilled, and the resulting product treated with a solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazone which precipitated, and which gave an m.p. of 145°, did not give depression when mixed with the 2,4-dinitrophenylhydrazone of acetyltrimethylene.

Reaction of Sulfuric Acid With Methylisopropylcyclopropylcarbinol (VIII)

10 g of the alcohol in 110 ml of sulfuric acid (1: 10) was heated to boiling, with vigorous stirring, for 1 hour. The reaction products were extracted with ether and washed with soda solution, followed by drying with potash. After removing the ether by distillation, the residue was twice distilled over metallic sodium to remove acetyltrimethylene impurity, small amounts of which were found to be present in the initial alcohol. A substance with b.p. 141 - 143° resulted, possessing a pleasant aroma.

n_D^{20} 1.4310; d_4^{20} 0.8624; MR_D 38.40. $C_8H_{16}O$. Calculated: MR_D 38.59.
Literature data for 2,2-methylisopropyltetrahydrofuran [10]: b.p. 142 - 143°; d_4^{21} 0.8690; n_D^{21} 1.4285; MR_D 37.93.

0.0990 g substance: 0.2714 g CO_2; 0.1115 g H_2O. Found %: C 74.82; H 12.60. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50.

The substance did not contain a hydroxyl group, was slowly oxidized by $KMnO_4$ solution (oxidation lasted for 48 hours). Neutral products did not result. The acid oxidation products were extracted with ether and dried with Na_2SO_4. After distilling off the ether, followed by distillation of the product, a substance with b.p. 97° at 8 mm (0.6 g) was isolated.

n_D^{20} 1.4500; d_4^{20} 0.9970; MR_D 38.29. $C_8H_{14}O$. Calculated: MR_D 38.60.
0.1083 g substance: 10 ml NaOH (T 0.003764): 1.5 ml HCl (T 0.003492).

0.1182 g substance: 0.0480 g Ag. Found: neut. equiv. 135.8; %: Ag 40.61. $C_8H_{14}O_2$. Calculated neut. equiv: 142; $C_8H_{15}O_3Ag$. Calculated %: Ag 40.45.

To determine neutralization equivalent, the substance was heated with 10 ml of alkali to complete dissolution, and the alkali excess titrated with hydrochloric acid. To obtain the silver salt, the lactone was dissolved in ammonia with heat, on a water bath, and ammonia excess removed by evaporation. Concentrated $AgNO_3$ was added to the resulting solution of ammoniacal salt of γ, δ-dimethyl-γ-hydroxycaproic acid. The precipitated silver salt was filtered off, washed with water and alcohol, and dried in a vacuum desiccator. Thus was obtained, as a result of oxidation of the substances with b.p. 141 - 143°, the lactone-γ, δ-dimethyl-γ-hydroxycaproic acid. Thus, there resulted on interaction of methylisopropylcyclopropylcarbinol with sulfuric acid, 2,2-methylisopropyltetrahydrofuran

Reaction of Sulfuric Acid With Glycol (IX)

10 g of 2,3-dicyclopropylbutandiol-2,3 was heated to boiling, with constant stirring, with 100 ml of dilute sulfuric acid (1: 10) for 1 hour. The liquid became very dark. After extraction of the reaction products with ether, following this by drying and removal of the solvent by distillation, there remained a dark, viscous oil, which resinified when attempt was made to distill it at 17 mm.

A second experiment was carried out with more dilute sulfuric acid (1: 15). The resulting light oil resinified upon distillation at 5 mm. A third experiment was carried out with the acid (1: 10) in a CO_2 atmosphere. Ether extractions of the reaction products were washed with soda solution and dried with Na_2SO_4. After distilling off the ether, the residue was distilled at 5 mm in a stream of CO_2. The following fractions resulted: 1st, 18 - 25°, 0.5 g; 2nd, 25°, 0.6g; the temperature then rose rapidly to 75°, and 1 g of distillate was collected; at 75°, all of the material remaining in the distilling flask immediately polymerized.

The fraction with b.p. 25° at 5 mm did not contain hydroxyl, did not decolorize $KMnO_4$ solution, and did give a 2,4-dinitrophenylhydrazone, with m.p. 181.5 - 182° (from alcohol).

n_D^{20} 1.4300; d_4^{20} 0.8678; MR_D 45.27; $C_{10}H_{16}O$. Calculated: MR_D 45.21.

0.0943 g substance: 0.2786 g CO_2; 0.0912 g H_2O. 0.1059 g substance; 12.41 g benzene: Δt 0.284°.

Found %: C 78.86; H 10.86; M 154.6. $C_{10}H_{16}O$. Calculated %: C 78.96; H 10.53; M 152.

Analysis of the 2,4-dinitrophenylhydrazone:

0.0962 g substance: 15.8 ml N_2 (17°; 767 mm). Found %: N 16.41. $C_{16}H_{21}O_4N_4$. Calculated %: N 16.81.

The substance boiling at 75°, 5 mm, was in the form of a mobile liquid of yellow color.

n_D^{20} 1.4790. 0.0317 g substance: 7.5 ml CH_4 (15.5°, 769 mm). Found: number of active hydrogens 2. $C_{10}H_{18}O_2$. Calculated: number of active hydrogens 2.

It was, in all probability, the unsaturated di-primary glycol (XII).

SUMMARY

1. The interaction of dimethylcyclopropyl-, methylethylcyclopropyl- and methylisopropylcyclopropylcarbinols with sulfuric acid has been studied.

2. It has been established that the first alcohol forms 2-methylpentene-3-ol-5, which then converts into 2,2-dimethyltetrahydrofuran and into the ester; the second alcohol gives 3-methylhexen-3-ol-6, 2,2-methylethyltetrahydrofuran and a mixture of unsaturated hydrocarbons; the third alcohol converts into 2,2-methylisopropyltetrahydrofuran.

3. It has been demonstrated that in the organomagnesium synthesis of methylisopropylcyclopropylcarbinol, there results the tertiary alcohol, 2,3-dicyclopropylbutandiol-2,3 which, when reacted with dilute sulfuric acid, converts into one of several possible ketones.

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• See Consultants Bureau Translation, page 437.
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INVESTIGATION IN THE FIELD OF COMPOUNDS CONTAINING THREE-MEMBERED OXIDE RINGS

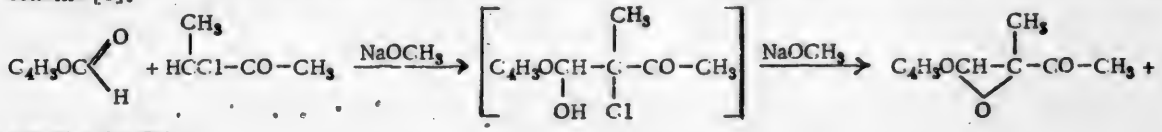
IX. CONDENSATION OF α-HALOKETONES WITH FURFURAL

V. F. Martynov

Several years ago the authors developed a new synthetic procedure for aliphato-aromatic α-ketoxides, produced by the condensation of aliphatic α-haloketones with benzaldehyde in the presence of sodium methylate [1]. The author has carried out condensation of benzaldehyde with chloroacetone, chloromethylketone and α-chloroethylmethylketone. The corresponding products resulted in good yields for all cases. This reaction was extended to other aliphatic α-haloketones [2].

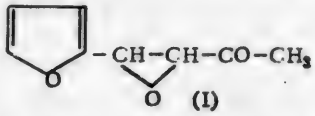
The present work has for its purpose an extension of this reaction to the field of heterocyclic aldehydes, of which, at present, only furfural has so far been used. The author carried out condensation of α-haloketones with furfural as in the case of benzaldehyde, and in the presence of sodium methylate.

The mechanism for a similar type of condensation reaction can be illustrated by the Claisen condensation scheme [3].

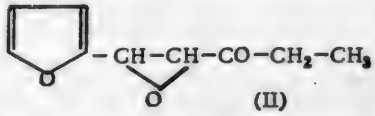


$+NaCl + CH_3OH.$

Condensation of furfural was carried out with chloroacetone, chloromethylethylketone, α-chloroethylmethylketone and chloroacetophenone. In all cases, reaction proceeded in a manner similar to that for benzaldehyde; however, not all of the condensation products were trapped. Thus, the condensation product of furfural with chloroacetone, which should have been furfuralacetone oxide (1-furyl-2-acetyl-oxide-ethane) (I) could not be isolated, despite several reruns of this reaction. Instead of an individual product, a resinous mass was obtained, which did not undergo fractionation. The same picture was observed when condensation of furfural with α-chloromethylethylketone was carried out The author did not succeed in obtaining 1-furyl-2-propionylethylene oxide (II):



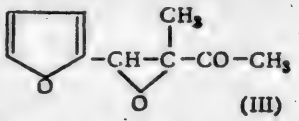
(I)



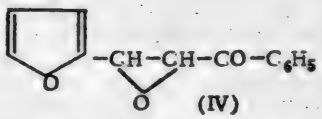
(II)

Instead of the expected compound, the author obtained a resinous mass. It should be mentioned that both reactions by external appearance apparently proceed normally, i.e., heat evolution and separation of a copious sodium precipitate were observed.

Only when condensing furfural with α-chloroethylmethylketone, did the author finally succeed in synthesizing an individual product – 1-furyl-2-methyl-2-acetyl-ethylene oxide (III). It should be mentioned that in the formation of this stable keto-oxide there was no such intense darkening of the reaction mixture as was the case in the preceding instances.



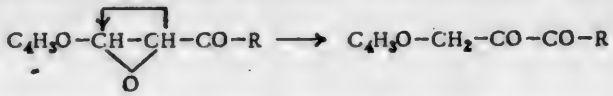
(III)



(IV)

On the grounds of the data, it might be assumed that the corresponding keto oxides were formed in the case of furfural with chloroacetone and α-chloromethylethylketone condensation, and that they could have resinified, however, in the presence of the alkaline reagent, sodium methylate.

This resinification can be represented as follows, via the preliminary formation from keto oxide of the α-diketone.



Similar isomerizations are known from the literature for aliphato-aromatic α-keto oxides, proceeding under the influence of various reagents, among them alkaline [4]. The resulting α-diketones, judging for example from 1-phenylbutandione-2,3, are quite unstable [5].

It might be expected, therefore, that this instability would be increased many-fold upon passing to diketones of the furfural series. If this point of view is taken, there can then be clarified as well the relatively high stability of 1-furyl-2-methyl-2-acetylethylene oxide. Formation of the α-diketone in such case would be difficult, since it is connected with replacement of a methyl group and not of a hydrogen.

1-Furyl-2-methyl-2-acetylethylene oxide (III) is a substance which is thermally quite stable; it distills readily in vacuo without noticeable resinification; all attempts to obtain the semicarbazone, however, failed; the crystalline derivative did not precipitate, and there was only observed a strong darkening of the reaction mixture. However, analyses, molecular weight, refraction and analogy in formation to the corresponding keto oxide of the benzaldehyde series [1] does not leave any doubts as to the structure of this compound.

Upon condensing furfural with chloroacetophenone, the author obtained furylbenzoyl-ethylene oxide (IV). Crystalline, colorless compound, changing readily in the air; after 2 - 3 days the crystals darkened and converted to a liquid. In the light of the above-presented concept, such a ready change becomes clear, since in this case isomerization to the corresponding α-diketone is quite possible.

EXPERIMENTAL

1-Furyl-2-methyl-2-acetylethylene Oxide (III) Synthesis

Freshly-distilled furfural and α-chloroethylmethylketone were used to carry out the reaction. 50 g of α-chloroethylmethylketone and 60 g of furfural were diluted with 50 ml of methyl alcohol. A solution of 10 g of sodium in 150 ml of methyl alcohol was added dropwise, with vigorous stirring, to the mixture cooled in ice water. After treatment of the reaction mixture with water, the oil which separated was extracted with ether. The ether extract was dried with sodium sulfate After distilling off the ether, the residue was fractionated twice in vacuo. 32 g of greenish-yellow liquid with b.p. 72 - 73° at 1 mm resulted. The yield was 41% of theory.

d_4^{16} 1.1384; n_α^{16} 1.49159; MR_α 42.27. $C_9H_{10}O_3$. Calculated MR_D 42.18.

0.1754 g substance: 0.4190 g CO_2; 0.0963 g H_2O. 0.1525 g substance: 0.3646 g CO_2; 0.0840 g H_2O. 0.2136 g substance; 17.11 g C_6H_6; Δt 0.39°. 0.0976 g substance; 17.11 g C_6H_6; Δt 0.18°. Found %: C 65.15, 65.2; H 6.10, 6.12; M 161.5, 158.1. $C_9H_{10}O_3$. Calculated %: C 65.06; H 6.02; M 166.

Furylbenzoylethylene Oxide (IV) Synthesis

10 g of chloroacetophenone was diluted with 15 ml of methyl alcohol, and 11 g of furfural then added. A solution of 1.5 g of sodium in 30 ml of methyl alcohol was added dropwise, with stirring, to the mixture cooled in ice water. No resinification was observed during the reaction; after completion of the condensation, a light-yellow liquid was formed, of weak alkaline reaction. A light precipitate of sodium chloride settled down to the bottom of the flask. The reaction mixture was treated with water, weakly acidified with acetic acid, and an ether extraction then made, which was dried with sodium sulfate. After distilling off the ether, the residue crystallized. The crystals isolated weighed 6 g (40%). For purification they were first crystallized from methyl alcohol and then from petroleum ether. Almost colorless crystals resulted with m.p. 58 - 59°.

0.0888 g substance: 0.2372 g CO_2; 0.0372 g H_2O. 0.1352 g substance: 0.3625 g CO_2; 0.0560 g H_2O. Found %: C 73.06, 73.12; H 4.67, 4.63. $C_{13}H_{10}O_3$. Calculated %: C 72.89; H 4.67.

SUMMARY

1. The condensation of furfural with chloroacetone, chloromethylethylketone, α-chloroethylmethylketone and chloroacetophenone in the presence of sodium methylate has been investigated.

2. The oxides of 1-furyl-2-methyl-2-acetylethylene and 1-furyl-2-benzoylethylene, unknown in the literature, have been synthesized and characterized.

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A STUDY OF HYDROXYDIHYDROFURANS

III. INTERACTION OF 2,4,5-TRIPHENYL-5-METHYL-2-HYDROXYDIHYDROFURAN 2,5 WITH ACETIC ANHYDRIDE

E. D. Venus-Danilova and A. N. Orlova

In the preceding article [1], the authors described properties for the interaction product between 2,4-diphenyl-5,5-dimethyl-2-hydroxyfuran -2,5 and acetic anhydride, and it was established that this substance is phenyl-(1-phenyl)-isocrotylacetoacetic acid.

Of interest was the question as to whether other substituted hydroxyhydrofurans are capable of similar reaction or not, and the problem of how stable the substituted acetoacetic acids formed during this reaction are with respect to the nature of radicals in the 5- position of the original hydroxydihydrofuran For solution of this problem, the authors selected 2,4,5-triphenyl-5-methyl-2-hydroxydihydrofuran -2,5 (I), which differs from the earlier-investigated hydroxydihydrofuran in the fact that one methyl radical in position 5 is replaced by the phenyl radical.

2,4,5-Triphenyl-5-methyl-2-hydroxydihydrofurane-2,5 was isolated, among other products, by reaction of 40% sulfuric acid with symmetrical methyldiphenylphenyl acetylenylethylene glycol (2,3,5-triphenylpentyne-4-diol-2,3) [2]. By interacting this hydroxydihydrofuran with acetic anhydride under conditions described in the preceding article [1], a crystalline substance of the empirical formula $C_{25}H_{22}O_5$ was obtained.

The substance possessed unsaturation (decolorization of aqueous potassium permanganate and bromine in chloroform), and acid properties - soluble in dilute aqueous alkali and carbonate solutions, and precipitated again by neutralization of the solutions Titration with alkali and determination of the number of active hydrogens indicated that the substance contained only one carboxyl group.

In contrast to the acid product described previously, which resulted from interaction of 2,4-diphenyl-5,5-dimethyl-2-hydroxydihydrofuran -2,5 with acetic anhydride, the ammoniacal salt of this compound did not precipitate upon passage of gaseous ammonia into an ether solution of the product.

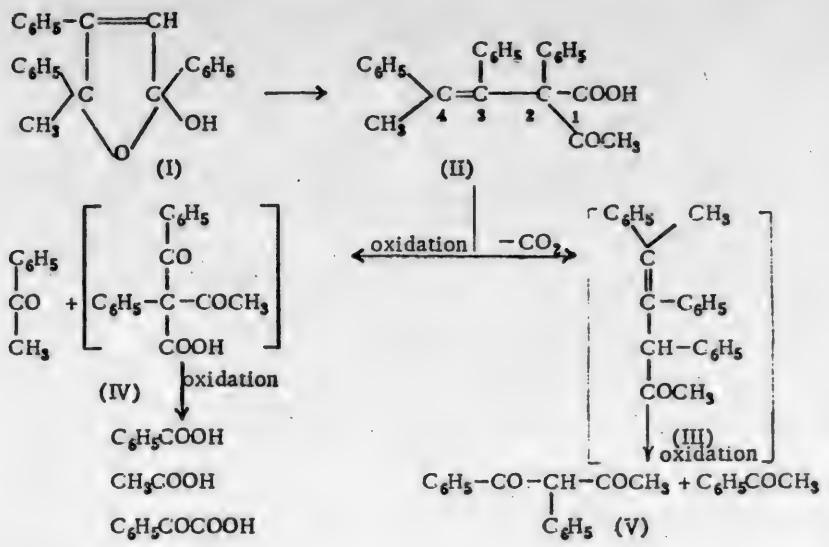
According to the standard reactions, no carbonyl group was found in the compound, to which the authors, by analogy with the acid previously obtained [1], attributed the structure of an unsaturated, substituted β-keto acid (II). A similar phenomenon was also observed previously for phenyl-(1-phenyl)-isocrotylacetoacetic acid.

The substance was oxidized with potassium permanganate in aqueous, weakly alkaline medium. Oxidation took place much more readily than for the analogous acid described earlier [1]. Upon oxidation in neutral medium, only carbon dioxide, acetophenone and the β-diketone – phenylacetylbenzoylmethane (1,2-diphenylbutandione-1,3) – were isolated; in alkaline medium, acetophenone, a smaller amount of the β-diketone, and very small amounts of formic, acetic, benzoic and benzoylformic acids were isolated. It is possible that in neutral medium rapid decarboxylation of the original acid proceeds, with formation of the unsaturated ketone (III), which upon oxidation, yields only neutral products. In alkaline medium, decarboxylation is slowed down, and therefore formation of acids (scheme) is also possible, along with neutral substances.

The fact that traces of formic acid were obtained can be explained by oxidation of the enolic form of β-diketone. (See top of next page).

However, the diketo acid (IV) and the unsaturated ketone (III) were not found among the oxidation products. On the other hand decarboxylation of the unsaturated β-keto acid (II) by boiling with water, or by heating in the dry state, was confirmed by carbon dioxide evolution.

Properties of the compound synthesized by the authors indicated that this substituted acetoacetic acid – 2,3,4-triphenyl-2-acetylpenten-3-acid (II) – was a considerably less stable compound than phenyl-(1-phenyl)-isocrotylacetoacetic acid, which evidently depends upon the presence of phenyl at carbon atom number 4 in the unsaturated acid molecule (II).



(I) (II) (IV) (III) (V)

EXPERIMENTAL

The initial 2,4,5-triphenyl-5-methyl-2-hydroxydihydrofuran-2,5 (m.p. 125 - 126°) was prepared according to the previous directions by one of us with L. A. Pavlova [2], in 21.6% yield, calculating on the basis of original acetylene α-glycol.

I. Synthesis and properties of $C_{25}H_{22}O_3$ Acid.

Upon heating a mixture of hydroxydihydrofuran and acetic anhydride to boiling (135 - 140°), considerable resinification was observed; this reaction, therefore, was carried out at lower temperature.

A solution of 1 g of hydroxydihydrofuran and 6 g of acetic anhydride was heated for 45 minutes on an oil bath at a temperature of 120°. Upon cooling, the light-yellow reaction mass was poured into 20 - 30 times the volume of ice water, with vigorous stirring; on standing, small lumps precipitated by the following day, which were ground in a mortar with water, and washed repeatedly with water (to a negative reaction for acid). After drying in air, a faintly-yellow compound, m.p. 82 - 83° (with decomp.) resulted. Because of its instablity, the substance failed to crystallize.

Synthesis of the substance was repeated several times under identical conditions.. 7.35 g of substance (86 %) was synthesized from 7.5 g of hydroxydihydrofuran, and after thorough washing with water, gave an m.p. of 82 - 83° (decomp.).

0.1114 g substance: 0.3298 g CO_2; 0.0608 g H_2O. 0.1001 g substance: 0.2965 g CO_2; 0.0541 g H_2O. Found %: C 80.74, 80.78; H 6.06, 6.00. $C_{25}H_{22}O_3$. Calculated %: C 81.08; H 5.95. 0.0837 g substance: 5.6 ml CH_4 (18°, 760 mm). Found: v_0 5.25 ml; % OH 4.78. $C_{25}H_{21}O_2(OH)$. Calculated v_0 5.07 ml; % OH 4.58.

0.0594 g substance: 1.9 ml 0.1 N NaOH (T 0.00400). No. of carboxyl groups found 1.2. $C_{25}H_{22}O_3$. No. of carboxyl groups calculated - 1.

The substance decolorized a solution of bromine in chloroform, and reacted with an aqueous solution of potassium permanganate. It did not react under standard conditions with semicarbazide, hydroxylamine or 2,4-dinitrophenylhydrazine.

II. Oxidation of $C_{25}H_{22}O_3$ acid.

a) Oxidation in weakly alkaline medium. 2.5 g of the substance, 0.3 g of sodium hydroxide, and 2 g of potassium permanganate solution in 100 ml of water were heated to 40° with vigorous stirring. After about 0.5 hours, decolorization had occurred, following which another 2 g of oxidant ground to a powder was added in 3 portions (according to theoretical calculations, 3.6 g of potassium permanganate would be required for 1 mole of initial substance, on the basis of 5 active oxygen atoms). Oxidation was complete after 2 hours.

The neutral oxidation products were removed from the manganese dioxide precipitate and from the filtrate by ether. After removal of the ether, the oily precipitate began to crystallize partially. All of the substance was converted to the semicarbazone, which, after recrystallization, melted at 195 - 196.5°, corresponding to acetophenone semicarbazone (mixed sample test). The yield of acetophenone, recalculated from 1 g of the semicarbazone, amounted to 0.7 g (86.4 %).

After isolation of the acetophenone, a stream of carbon dioxide was passed into the aqueous solution to tie up excess alkali and to decompose the diketone enolate, after which the neutral oxidation products volatile with

steam were distilled into a solution of p-nitrophenylhydrazine. A yellow precipitate resulted immediately, with m.p. 136 - 137°, corresponding to the pyrazole obtained from the β-diketone – acetylbenzoylphenylmethane (mixed sample test) – described in Communication I.

No other products were found in the ether extract obtained from the residue after distilling the β-diketone.

Benzoylformic acid was found in a sample of the organic salt solution (the formation of a yellow interaction product with phenylhydrazine hydrochloride, with m.p. 153° [3]). After concentrating the salt solution on a water bath, and decomposing it with dilute sulfuric acid, a small amount of benzoic acid (about 0.07 g) was obtained by sublimation, which was characterized by its m.p. and by mixed sample. Traces of formic acid were found in the filtrate distillate (turbidity of mercuric chloride solution, blackening of silver nitrate).

A small amount of silver salts was obtained from the second and third fractions of the distillate, turning black upon heating, decomposed and removed by repeated boiling and filtration. The silver content – silver acetate – was determined in the residue (about 0.08 g). Found %: Ag 64.89. $C_2H_3O_2Ag$. Calculated %: Ag 64.65.

b) Oxidation in neutral medium. 2.5 g of the substance was oxidized with 100 ml of an aqueous solution of potassium permanganate (1.4 g theoretically required, calculating on the basis of 2 active oxygen atoms per mole of substance) at a temperature of 40°. Reaction time was 2 hours. The carbon dioxide evolved during reaction was trapped in a Tishchenko flask with baryta water. The ether extract of filtrate and precipitate was washed with 30 ml of 3% sodium hydroxide solution to separate the β-diketone. After evaporation of the ether, actophenone resulted, characterized as its semicarbazone, with m.p. 195 - 196°. 0.52 g of semicarbazone resulted, corresponding to a 70% yield of acetophenone.

After extraction of acetophenone, the alkaline solution was neutralized with dilute sulfuric acid, and acetylbenzoylphenylmethane volatile with steam was distilled out of the solution and extracted with ether. After distilling off the ether, 0.75 g of a paraffin-like mass was separated, which solidified into a substance with m.p. 90 - 92°, found from its properties to be identical with acetylbenzoylphenylmethane described in the preceding article [1]. Pyrazole obtained from it had an m.p. of 137 - 138°, corresponding to the pyrazole described in preceding experiments (mixed sample).

Upon acidification of a concentrated aqueous solution of organic acid salts, obtained after removal of the neutral oxidation products, 0.9 g of the initial compound was obtained. After its separation from the filtrate, no organic acids were found, except for traces of formic acid.

SUMMARY

1. By reaction of acetic anhydride with 2,4,5-triphenyl-5-methyl-2-hydroxydihydrofuran - 2,5, the β-keto acid $C_{25}H_{22}O_3$ – 2,3,4-triphenyl-2-acetylpenten-3 acid has been synthesized.

2. It has been established that this acid is considerably less stable than phenyl(1-phenyl)-isocrotylacetoacetic acid, described earlier.

3. An assumption has been made that a decrease in stability of the acid obtained depends upon the presence of a phenyl group in the 5-position of hydroxyhydrofuran.

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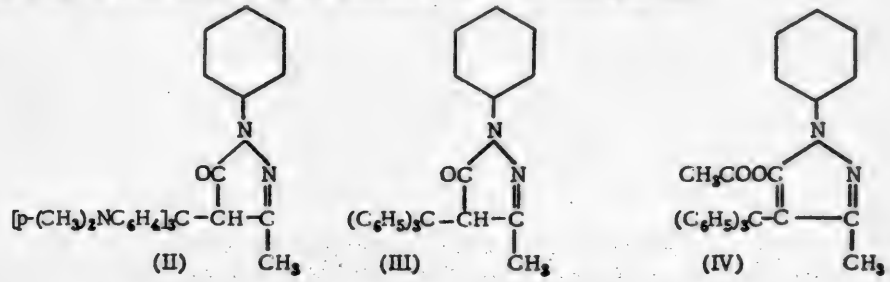
* See Consultants Bureau Translation, page 707.
** " " " " " a-197.

CONDENSATION PRODUCTS OF TRIPHENYLCARBINOLS WITH 1-PHENYL-3-METHYLPYRAZOLONE-5. II.

O. F. Ginzburg

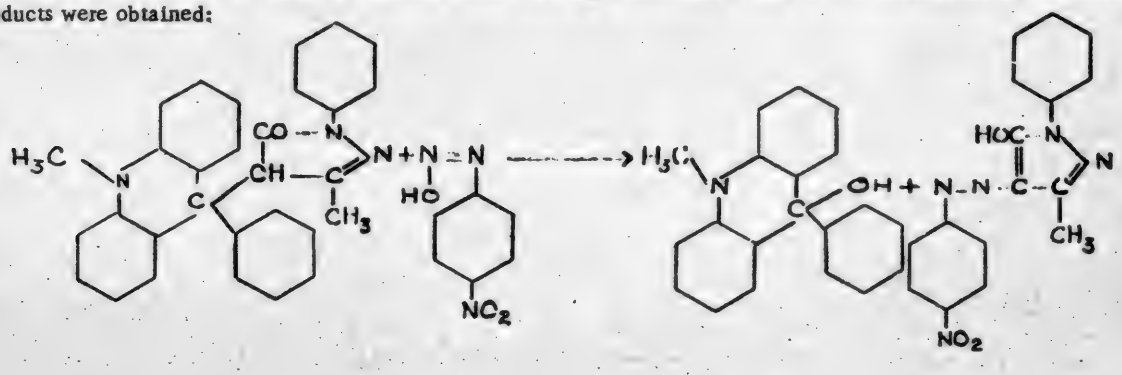
It was demonstrated in the preceding article [1] that 4,4'-tetramethyldiaminotriphenylcarbinol enters readily into a condensation reaction with 1-phenyl-3-methylpyrazolone-5. This is explicable on the basis that 4,4'-tetramethyldiaminotriphenylcarbinol contains quite a mobile hydroxyl group; it might therefore be expected that 9-phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine, in which the hydroxyl group is quite mobile, would, in its turn, enter readily into condensation with 1-phenyl-3-methylpyrazolone-5. Experiments carried out have confirmed this assumption: 1-phenyl-3-methyl-4-(9'-phenyl-10'-methyl-9',10'-dihydroacridyl-9')-pyrazolone-5 (I) was formed in almost 90% yield upon heating in methyl alcohol equimolecular amounts of 9-phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine and 1-phenyl-3-methylpyrazolone-5. Compound (I) was an almost colorless, crystalline substance, and upon its dissolution in polar solvents, colored solutions were formed. Thus, for example, a solution of compound (I) in glacial acetic acid was colored yellow, in nitrobenzene it was colored orange. Coloration of the above-indicated solutions attests to the decomposition of compound (I) into ions resulting from rupture of the bond between the 9'-carbon atom of the acridine part of the molecule, and the 4-carbon atom of the pyrazolone ring.

Condensation of aminotriarylcarbinols, or of their methyl esters, with 1-phenyl-3-methylpyrazolone-5 also proceeds in benzene. Thus, for example, when a benzene solution containing equimolecular amounts of the methyl ester of 4,4',4''-hexamethyltriaminotriphenylcarbinol and 1-phenyl-3-methylpyrazolone-5 was heated, 1-phenyl-3-methyl-4-(p,p',p''-hexamethyltriaminotriphenylmethyl)-pyrazolone-5 (II) was formed, which was isolated from the benzene solution by dilution of the latter with gasoline.



Upon dissolution of (II) in glacial acetic acid, nitrobenzene, alcohol, and other polar solvents, violet-colored solutions resulted.

As with other compounds [2], which contain the 1-phenyl-3-methyl pyrazolone-5 radical, (I) and (II) reacted with the diazo compound. Thus, for example, upon reacting compound (I) with p-nitrodiazobenzene, the following products were obtained:



This reaction also bears out the lability of the bond between the acridine and pyrazolone parts of the molecule.

It was mentioned in the preceding article that triphenylcarbinol in alcohol medium does not enter into condensation with 1-phenyl-3-methylpyrazolone-5. Further experiments indicated that under more rigorous conditions, namely in glacial acetic acid medium, triphenylcarbinol reacts with 1-phenyl-3-methylpyrazolone-5. In this case 1-phenyl-3-methyl-4-triphenylmethylpyrazolone-5 (III) is formed. Compound (III) acylated with acetic anhydride. Resulting from the acylation was 1-phenyl-3-methyl-4-triphenylmethyl-5-acetoxypyrazole (IV), which was also obtained by heating equimolecular amounts of triphenylcarbinol and 1-phenyl-3-methylpyrazolone-5 in acetic anhydride. As with compounds (I) and (II), compound (III) entered into reaction with diazo compounds; in this case, the triphenylcarbinol and pyrazolone azo dye were formed.

EXPERIMENTAL

1-Phenyl-3-methyl-4-triphenylmethylpyrazolone-5

1.95 g of triphenylcarbinol and 1.50 g of 1-phenyl-3-methylpyrazolone-5 were dissolved in 10 ml of glacial acetic acid, to which had been added beforehand 3 drops of concentrated hydrochloric acid. The resulting solution was boiled for 3 hours in a flask with reflux condenser. After cooling, there precipitated from the solution a precipitate which was filtered and then dried. The precipitate was boiled with 40 ml of alcohol. After cooling, the portion which did not dissolve in alcohol was filtered and dried. 0.95 g of substance with m.p. 208 - 210° resulted. The compound obtained was dissolved in 40 ml of a 0.3% alcoholic solution of potassium hydroxide. Upon acidification of the resulting solution with acetic acid, a precipitate formed which was filtered and dried. 0.90 g of substance, with m.p. 209 - 211° resulted. A second precipitation of the compound, as well as recrystallization from alcohol, did not result in any increase of the melting point.

0.1162 g substance: 0.3408 g CO_2; 0.0606 g H_2O. 0.1102 g substance: 6.7 ml N_2 (20°, 758 mm).
Found %: C 83.30; H 6.07, N 7.01. $C_{25}H_{20}ON_2$. Calculated %: C 83.60; H 5.81; N 6.73.

1-Phenyl-3-methyl-4-triphenylmethyl-5-acetoxypyrazole

3.00 g of 1-phenyl-3-methylpyrazolone-5 and 3.90 g of triphenylcarbinol were dissolved in 20 ml of acetic anhydride, to which 5 drops of concentrated hydrochloric acid had been added beforehand. The resulting solution was heated for 3 hours on an oil bath (bath temperature 150 - 160°). Upon cooling there resulted a crystalline white precipitate from the solution, which was filtered and dried. 5.67 g of substance with m.p. 234° resulted. The yield was 88.4% of theory. The m.p. was 236° after recrystallization from alcohol or benzene.

0.1973 g substance: 10.4 ml N_2 (22°, 764 mm). 0.1992 g substance: 10.5 ml N_2 (20°, 763 mm).
Found %: N 6.07, 6.11. $C_{31}H_{26}N_2O_2$. Calculated %: N 6.10

0.1 g of 1-phenyl-3-methyl-4-triphenylmethylpyrazolone-5 was dissolved in 5 ml of acetic anhydride, to which one drop of concentrated hydrochloric acid had been added beforehand. The resulting solution was heated for 3 hours on an oil bath (bath temperature 150 - 160°). The reaction mixture was poured into water, and on the following day the precipitate which had formed was filtered off. The melting point of the resulting compound was 234 - 236°. A sample mixed with 1-phenyl-3-methyl-4-triphenylmethyl-5-acetoxypyrazolone (m.p. 236°) melted at 234 - 236°.

1-Phenyl-3-methyl-4-(9'-phenyl-10'-methyl-9',10'-dihydroacridyl-9')-pyrazolone-5.

1.42 g of 9-phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine (0.005 mole) and 0.87 g of 1-phenyl-3-methylpyrazolone-5 (0.005 mole) were dissolved in 40 ml of alcohol, and the resulting solution was boiled for 20 minutes on a water bath. The precipitate formed was filtered off, washed with alcohol, and dried. 1.95 g of substance, with m.p. 188°, was obtained. After crystallization from alcohol, the melting point of the compound obtained remained unchanged Yield was 88.7% of theory.

0.1400 g substance: 0.4180 CO_2; 0.0723 H_2O. 0.1206 g substance: 10.0 ml N_2 (24°, 763 mm).
Found %: C 81.43; H 5.78; N 9.47. $C_{30}H_{25}ON_3$. Calculated %: C 81.26; H 5.69; N 9.48.

0.44 g of 1-phenyl-3-methyl-4-(9'-phenyl-10'-methyl-9',10'-dihydroacridyl-9')-pyrazolone-5 (0.001 mole) and 1 g of sodium acetate were dissolved in 12 ml of glacial acetic acid. 5 ml of 0.2M solution of p-nitrophenyldiazonium chloride was added to the resulting solution. A dye precipitate formed immediately, which was filtered

off and dried. 0.25 g of azo dye was obtained, which, after recrystallization from glacial acetic acid, melted at 198°. A mixed sample of the azo dye obtained with that resulting from interaction of 1-phenyl-3-methylpyrazolone-5 with p-nitrophenyldiazonium (m.p. 198°), melted at 198°.

The acetate filtrate was mixed with 100 ml of 20% potassium hydroxide solution. The precipitate which formed was filtered off, washed with water and dried. 0.25 g of substance with m.p. 135 - 136° resulted. A sample of the obtained compound when mixed with 9-phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine (m.p. 140°), melted at 136°.

Upon reacting p-nitrophenyldiazonium with 1-phenyl-3-methyl-4-triphenylmethylpyrazolone-5, with 1-phenyl-3-methyl-4-(p-dimethylaminotriphenylmethyl)pyrazolone-5, with 1-phenyl-3-methyl-4-(p,p'-tetramethyldiaminotriphenylmethyl)-pyrazolone-5, and with 1-phenyl-3-methyl-4-(p,p',p"-hexamethyltriaminotriphenylmethyl)-pyrazolone-5, respectively, the corresponding triphenylcarbinols, and the pyrazolone dye, were formed.

1-Phenyl-3-methyl-4-(p,p',p"-hexamethyltriaminotriphenylmethyl)-pyrazolone-5.

2.01 g of the methyl ester of 4,4',4"-hexamethyltriaminotriphenylcarbinol (0.0005 mole) and 0.87 g of 1-phenyl-3-methylpyrazolone-5 (0.0005 mole) were dissolved in 15 ml of benzene, and the resulting dark-violet solution boiled for 1 hour. After cooling, 120 ml of gasoline was added to the benzene solution. A precipitate formed, which was filtered off and dried. 0.9 g, with m.p. 154 - 156° resulted.

0.0712 g substance: 8.2 ml N_2 (25°, 750 mm), 0.1136 g substance: 12.8 ml N_2 (24°, 756 mm).
Found %: N 12.87, 12.74. $C_{35}H_{39}ON_5$. Calculated %: N 12.84.

SUMMARY

1. Triphenylcarbinol enters into a condensation reaction with 1-phenyl-3-methylpyrazolone-5- under more rigorous conditions than for 9- hydroxy-9-phenyl-10-methyl-9,10-dihydroacridine or the methyl ester of 4,4',4"-hexamethyltriaminotriphenylcarbinol.

2. Upon reacting diazo compounds with condensation products of triarylcarbinols and with 1-phenyl-3-methyl-pyrazolone-5, there are formed triarylcarbinol and pyrazolone azo dyes.

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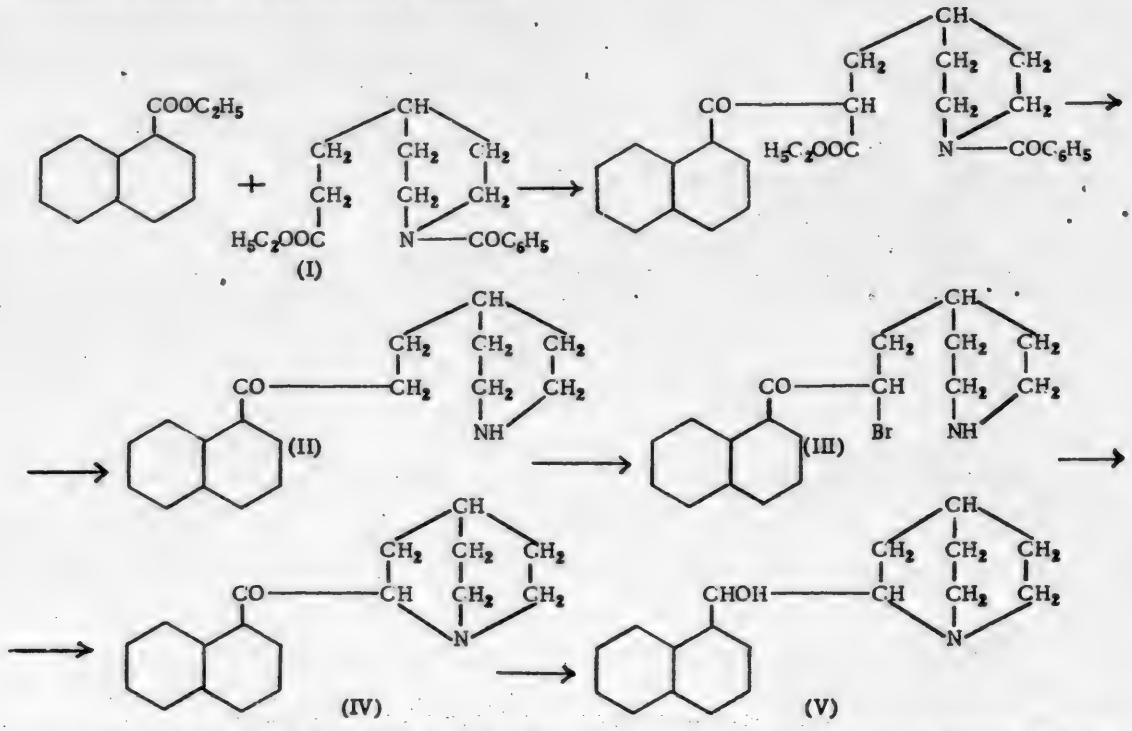
* See Consultants Bureau Translation, page 1103.

[QUINUCIYDYL-(2)]-[NAPHTHYL-(1)]-CARBINOL. VII.

V. M. Rubtsov and V. A. Volskova

A study of hydroquinine and its pyridine analogs [1] has indicated that the activity of compounds of the quinine-type alkaloids is related not so much to the quinoline nucleus as to the position of the quinuclidic radical in this ring. Thus, for example, rearrangement of the quinoeuclidic radical to the number 2 or 8 position of the quinoline ring results in a loss of chemotherapeutic action, at the same time that replacement of the quinoline ring by the corresponding pyridine ring (pyridyl-4) affects but little the chemotherapeutic index. Hence, the presence of a quinoline ring is not strictly required for exhibiting antimalarial action in compounds of this type, and by appropriate selection of another radical, active preparations can be obtained.

This concept has served as the basis for synthesizing [quinuclidyl-(2)]-[naphthyl-(1)]-carbinol, which was synthesized according to the following scheme:



Upon condensing the ethyl ester of α-naphthoic acid and the ethyl ester of β-[N-benzoylpiperidyl-(4)]-propionic acid, there resulted the keto ester (I). The reaction proceeded less readily than with the corresponding quinoline derivatives, and the yield of keto ester did not exceed 24%. Saponification of the keto ester with 17% hydrochloric acid gave unsatisfactory results; reaction proceeded readily only when a mixture consisting of equal volumes of alcohol and of concentrated hydrochloric acid was used. [β-(Piperidyl-(4))-ethyl]-[naphthyl-(1)]-ketone (II) which resulted in this case was in the form of a yellow oil, forming a crystalline hydrochloride with m.p. 173.5 - 175°, when mixed with an alcoholic solution of hydrogen chloride. This compound, when treated with bromine in 48% hydrobromic acid, converted into the bromoketone (III), which cyclized readily upon reacting with sodium bicarbonate, to form [quinuclidyl-(2)]-[naphthyl]-(1)]-ketone (IV). Reduction of the carbonyl group to carbinol was carried out by hydrogenation of the ketone hydrochloride in aqueous medium in the presence of palladium black. From the hydrogenation product, which represented a mixture of four stereoisomeric carbinols (V), two diastereoisomeric racemates were isolated, whose properties are given in the Table.

Racemate	Base	Hydrochloride	Characteristic
A	White needles, m.p. 200 - 201°	White crystalline powder, m.p. 203.5 - 205.5°	Base very poorly soluble in ether
B	White prisms, m.p. 63 - 65°	White crystalline powder, m.p. 267.5 - 269°	Base readily soluble in ether

The racemates obtained, in contrast to the quinic alkaloids, did not change when boiled with 50% acetic acid.

Both racemates were found to be inactive when tested on green finches infected with Plasmodium relictum

EXPERIMENTAL

[β-(Piperidyl-(4))-ethyl]-[naphthyl-(1)]-ketone (II).

10 g of the ethyl ester of α-naphthoic acid was added to sodium ethylate obtained from 1.23 g of powdered metallic sodium and 2.46 g of absolute alcohol in an absolute ether medium. The mixture was slowly heated on an oil bath to 100°, with simultaneous distilling off of the ether. When the bath temperature rose to 100°, 8.5 g of the ethyl ester of β-[N-benzoyl-piperidyl-(4)]-propionic acid was added to the reaction mixture and the mixture stirred at the indicated temperature for 19 hours The bath temperature was then lowered to 70°, andto the reaction mixture was added 50 ml of benzene, and the mixture allowed to cool while being stirred.

After cooling, the reaction mixture was shaken in a separatory funnel with 200 ml of ice water. The water layer was separated from the benzene layer, washed with ether, and treated with 10% sulfuric acid to a neutral reaction with litmus paper. The resulting oil was extracted with chloroform, and the extract dried with anhydrous sodium sulfate. After distilling off the solvent, and removing the residue in vacuo, there resulted 3.2 g of β-[N-benzoyl-piperidyl-(4)]-α-carboethoxyethyl-[naphthyl-(1)]-ketone (keto ester) in the form of a yellow viscous oil. Yield was 23.6% of theory.

Without further purification, the resulting keto ester was subjected to ketonic rupture by boiling for 3 hours with 20 times the amount of a mixture consisting of equal volumes of alcohol and concentrated hydrochloric acid.

Upon termination of heating, the alcohol was distilled off in vacuo, the hydrochloric acid solution washed with ether to remove benzoic acid, and made alkaline with an excess of 50% potash. The resulting oil was extracted with ether and the extract dried with potash. After distilling off the solvent, 1.84 g of a yellow oil, found to be the [β-(piperidyl-(4))-ethyl]-[naphthyl-(1)]-ketone was obtained. Yield was 73.8% of theory, calculating on the basis of keto ester.

Upon reacting an alcoholic solution of hydrogen chloride with the ketone in acetone solution, the hydrochloride formed, which, after recrystallization from absolute alcohol, was in the form of white needles with light yellow tint. M.p. 173.5 - 175°.

The hydrochloride was readily soluble in water and absolute alcohol (approximately 1: 10), and insoluble in acetone and ether.

3.295 mg substance: 8.579 mg CO_2; 2.095 mg H_2O. 7.815 mg substance: 0.323 ml N_2 (20°, 737 mm). Found %: C 71.01; H 7.11; N 4.66. $C_{19}H_{21}ON \cdot HCl$. Calculated %: C 71.14; H 7.30; N 4.61.

Hydrobromide of [β-(piperidyl-(4))-α-bromoethyl]-[naphthyl-(1)]-ketone (III)

1.03 g of bromine in 10 ml of 48% hydrobromic acid was added to a solution of 1.97 g of piperidylethyl-naphthylketone hydrochloride in 12 ml of 48% hydrobromic acid heated at 70°, over a period of 10 minutes with stirring. The temperature was then increased to 80°, and stirring continued for another 25 minues. Upon cooling, a precipitate formed, which was filtered off, washed with water, acetone, and dried in the air; yellow, crystalline powder, melting at 189 - 190°. Readily-soluble in chloroform, poorly so in water; insoluble in acetone and ether. Yield was 2.45 g (88.4%).

7.119 mg substance: 6.272 mg AgBr. 6.703 mg substance: 5.899 mg AgBr. Found %: Br 37.48, 37.45. $C_{18}H_{20}ONBr \cdot HBr$. Calculated %: Br 37.43.

[Quinuclidyl-(2)]-[naphthyl-(1)]-ketone (IV).

2.3 g solution of β-[piperidyl-(4)]-α-bromoethyl-[naphthyl-(1)]-ketone hydrobromide in 30 ml of chloroform was mixed with 2.5 g solution of sodium bicarbonate in 30 ml of water. The mixture was shaken for 2.5 hours. The chloroform layer was then separated from the water layer and dried with potash. After evaporation of the chloroform, the residue was recrystallized frompetroleum ether. 0.86 g of quinuclidylnaphthylketone resulted in the form of white, prismatic platelets of yellow tint, melting at 98.5 - 100°. Yield was 60% of theory.

The substance was readily-soluble in alcohol, chloroform, ether and acetone; soluble in hot petroleum ether, insoluble in water.

4.076 mg substance: 12.133 mg CO_2; 2.624 mg H_2O. 5.783 mg substance: 0.282 ml N_2 (17.5°, 733.8 mm). Found %: C 81.18; H 7.20; N 5.52. $C_{18}H_{19}ON$. Calculated %: C 81.46; H 7.22; N 5.28.

Hydrochloride – white platelets (from water), m.p. 246 - 247°; readily soluble in alcohol and chloroform, soluble in water, insoluble in acetone and ether.

6.905 mg substance: 3.316 mg AgCl. Found %: Cl 11.88. $C_{18}H_{19}ON \cdot HCl$. Calculated %: Cl 11.76.

[Quinuclidyl-(2)]-[naphthyl-(1)]-carbinol (V)

1.62 g of the above-obtained ketone was dissolved in 6.19 ml of 1N hydrochloric acid and 30 ml of water. 10 ml of 2% palladium chloride was added to the solution; a pink precipitate resulted which dissolved upon shaking. The solution obtained was hydrogenated at room temperature. After completion of hydrogenation, the solution was filtered off from the catalyst and treated with excess 50% potassium hydroxide solution. The resulting base was extracted with ether 4 times, using 125 ml portions, and the extract dried with potash. The ether solution was then concentrated to 25 ml volume. White crystals in the form of white needles precipitated. The crystals were filtered off and washed with ether. 0.37 g was obtained; m.p. 200 - 201°.

The substance was readily soluble in alcohol and acetone, very poorly in ether, insoluble in water. Recrystallization from acetone did not increase the melting point. This substance, according to analysis, was the quinuclidylnaphthyl (racemate A).

3.400 mg substance: 10.143 mg CO_2; 2.339 mg H_2O. 2.828 mg substance: 8.380 mg CO_2; 2.004 mg H_2O. 8.136 mg substance: 0.372 ml N_2 (24°, 728 mm). Found %: C 80.82, 80.81; H 7.70, 7.92; N 5.03. $C_{18}H_{21}ON$. Calculated %: C 80.85; H 7.84; N 5.24.

Hydrochloride. A white, crystalline powder, with m.p. 203.5 - 205.5°. Readily soluble in water, alcohol, chloroform and acetone; insoluble in ether.

Another 0.08 g of the less pure racemate A, with m.p. 194 - 197° resulted from the mother liquor upon additional evaporation, and 1.08 g of a light-yellow oil, readily soluble in ether. The oil was mixed with a calculated amount of 14% alcoholic hydrogen chloride solution, calculated on the basis of hydrochloride. The mixture was evaporated in vacuo to dryness, the residue mixed with 4 ml of dry acetone, and the resulting precipitate filtered off and washed with acetone and ether. 0.92 g of hydrochloride, melting at 249 - 251° resulted.

For the purification, the hydrochloride was dissolved in a small volume of absolute alcohol, and was isolated from solution by addition of dry acetone. Yield was 0.6 g.

Hydrochloride. A white, crystalline powder with m.p. 267.5 - 269°. Readily-soluble in water, alcohol, chloroform; insoluble in dry acetone and ether According to analysis, this substance was found to be the quinuclidylnaphthylcarbinol hydrochloride (Racemate B hydrochloride).

3.037 mg substance: 7.919 mg CO_2; 2.006 mg H_2O. 3.700 mg substance: 9.672 mg CO_2; 2.386 mg H_2O. 7.136 mg substance: 0.314 ml N_2 (24°, 728 mm). Found %: C 71.11, 71.29; H 7.38, 7.21; N 4.84. $C_{18}H_{21}ON \cdot HCl$. Calculated %: C 71.14; H 7.30; N 4.61.

The free base was isolated from the hydrochloride as a colorless oil which crystallized after standing 2 days in a vacuum desiccator over potassium hydroxide. Melting point of the crystals was 63 - 65°. The base was readily soluble in alcohol, acetone, ether and chloroform.

The resulting diastereoisomeric racemates A and B, in contrast to the quinic alkaloids, do not change with boiling in 50% acetic acid.

SUMMARY

1. [Quinuclidyl- -(2)]-[naphthyl-(1)]-ketone has been synthesized.

2. Upon catalytic hydrogenation of the indicated ketone, there is formed a mixture of two diastereoisomeric racemates, which have been separated by virtue of their differential solubility in ether.

3. The racemates obtained, in distinction to the quinic alkaloids, do not change when boiled with 50% acetic acid

4. Both racemates have been found inactive when tested on green finches infected with Plasmodium relictum.

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RELATIONSHIP BETWEEN THE QUANTITY OF HYDROGEN BROMIDE EVOLVED AND THE STRUCTURES OF BROMINATED OLEFINS

A. A. Petrov

In determining the degree of unsaturation for hydrocarbons by the volume of bromine added, a certain amount of hydrogen bromide ("abnormal bromination") is usually formed. Despite the fact that many works have been devoted to problems of halogenation of unsaturated compounds, quantitative data have nevertheless been very few regarding the formation of hydrogen halide acids in relation to the initial unsaturated hydrocarbon. Thus, V. I. Esafov [1] investigated bromination of certain dienes, wherein he noted formation of a larger amount of hydrogen chloride than upon bromination of olefins.

In the present work, there have been investigated a large number of cases relating the quantity of hydrogen bromide evolved to the structure of brominated olefins. Bromination was carried out with 1% Br solution in methanol, saturated with NaBr. Bromination, as carried out above, almost excludes the possibility of hydrogen bromide evolution by substitution reaction [2]. Data obtained on formation of hydrogen bromide, given in mol per cent hydrogen bromide, are related to the quantity of bromine used, and are presented in the Table.

Hydrocarbon (Group I)	HBr (mol %)	Hydrocarbon (Group II)	HBr (mol %)	Hydrocarbon (Group III)	HBr (mol %)
Hexene-1	16.1	2-Methylpentene-2	29.4	2,4-Dimethylpentene-2	42.2
Heptene-1	16.4	3-Methylpentene-2	29.2	3,4-Dimethylhexene-2	40.3
Octene-1	16.3	2-Methylhexene-2	30.4	2,4-Dimethylhexene-4	53.6
Nonene-1	16.4	3-Methylhexene-3	29.3	2,4,4-Trimethylpentene-1	46.0
Decene-1	16.9	3-Ethylpentene-2	27.5	2,2,3-Trimethylpentene-3	44.0
Dodecene-1	15.6	4-Methylheptene-3	30.7	2,3,4-Trimethylpentene-2	75.0
Tridecene-1	15.8	2-Ethylhexene-1	29.2	2,2,3-Trimethylhexene-3	41.5
Hexadecene-1	17.0	3-Ethylhexene-2	29.5	Triisobutylene	60.3
Heptene-3	15.5	5-Methylnonene-4	28.5	1-Cyclohexylcyclohexene-1	55.0
Nonene-4	15.1	4-Propylheptene-3	34.0	Note. The data given do not take into account hydrogen bromide in the original solution.	
Cyclohexene	16.7	2,3-Dimethylbutene-2	29.6		
3-Methylcyclohexene-1	18.8	2,5-Dimethylhexene-2	28.2		
Allylcyclohexane	16.5	2,3,3-Trimethylbutene-1	26.1		
Allylbenzene	10.0	1-Methylcyclohexene-1	26.3		
4-Methylpentene-1	16.1	1-Ethylcyclohexene-1	26.1		
5-Methylhexene-1	14.0	1-Propylcyclohexene-1	28.3		
6-Methylhexene-1	14.9	1-Butylcyclohexene-1	29.4		
3,3-Dimethylbutene-1	14.0	1-Methylcyclopentene-1	40.0		
4,4-Dimethylpentene-1	17.8	1-Ethylcyclopentene-1	40.2		
4,4-Dimethylhexene-1	18.7	1-Butylcyclopentene-1	38.5		

As can be seen from data given in the Table, unsaturated hydrocarbons can be divided into three groups; differing in the amount of hydrogen bromide evolved during bromination. The first group consists of hydrocarbons, linear in structure, as well as branched hydrocarbons with the alkyl side chain isolated from the double bond. Here too, belong cyclic hydrocarbons with analogous distribution of the multiple bonds. For this overall group of hydrocarbons, a small and approximately equal (for each olefin) volume of hydrogen bromide evolution is characteristic, fluctuating within the range 14 - 16 mol %. The second group consists of hydrocarbons with branching at the position of the double bond, i.e., hydrocarbons with a tertiary double bond, polarized, and already possessing known steric hindrance To this group are also related the cycloolefins which have an analogous structure. For all hydrocarbons of the second group, the approximately equal formation of hydrogen bromide is characteristic, fluctuating

in the range 27 - 29% (for the five-membered cyclenes, in the range 38-40%). Finally, a third group of hydrocarbons is characterized by considerably greater evolution of hydrogen bromide. To this group belong the branched hydrocarbons with one part of the tertiary bond groups creating steric hindrance (isopropyl, sec.-butyl, ter.-butyl). There is no clear-cut mechanism as to the amount of hydrogen bromide evolved when hydrocarbons of this group are brominated, since the amount of hydrogen bromide formed fluctuates within a rather large range (from 41 to 75 mol %).

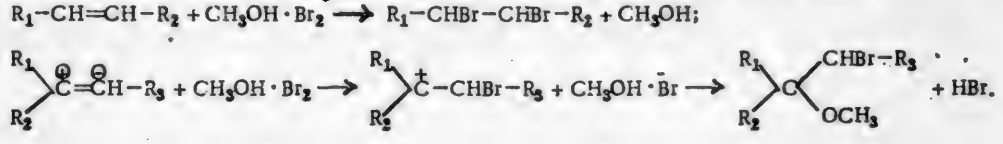
The rather considerable difference in amount of hydrogen bromide evolved upon bromination of hydrocarbons of Groups I and II makes it possible to solve the reverse problem: according to the amount of hydrogen bromide evolved, the content of olefin with tertiary double bond among the products that brominate is calculated. Experiments carried out with synthetically-prepared olefin mixtures of normal structure, and olefins with a tertiary double bond, have indicated that hydrogen bromide evolution is in proportion to the content of branched hydrocarbons in the mixture. It is understood that the presence of olefins with a tertiary group may distort considerably the analytical results.

To conclude, we shall consider the reaction mechanism for hydrogen bromide formation. There are indications in the literature that upon brominating with a methanol solution of bromine, aside from the usual halogen addition at the double bond, there also proceeds an abnormal bromination reaction, with formation of methoxymonobromides of the initial hydrocarbon [3, 4, 5].

The author also found methoxymonobromides among the bromination products.

Since formation of hydrogen bromide and methoxybromide proceeds with particular intensity upon bromination of olefins with tertiary double bonds, the author was therefore attracted to the use of a known scheme for chlorination of tertiary olefins according to Lvov-Tishchenko [6, 7] for a clarification of the bromination mechanism. Considering that the halogenating agent in the author's case is a molecular compound of bromine and methyl alcohol, and not of bromine alone, the bromination reaction can be represented on the whole as follows:

I) $R_1-CH=CH-R_2 + CH_3OH \cdot Br_2 \longrightarrow R_1-CHBr-CHBr-R_2 + CH_3OH;$

II) 

First of all, the initial hydrocarbon does not possess branching at the double bond, and hence polarization of the molecule is negligible, and the predominant direction for the bromination reaction is the usual addition of bromine at the double bond (classical scheme).

In the second case, the brominated olefin has a tertiary double bond, and hence the hydrocarbon molecule is polarized. Therefore, in this case, as well as with chlorination according to the Lvov-Tishchenko reaction, halogen addition is noted as deviating from the classical addition scheme, and also, in contrast to chlorination, proceeds almost quantitatively along the abnormal route, the extent of abnormal reaction in the given case depending entirely upon the structure of the hydrocarbon brominated, and, as has already been mentioned, fluctuating within the range 25 - 75% (see Table).

It is quite characteristic that the value for abnormal bromination increases noticeably in those cases where, in the hydrocarbon molecules, there are present radicals attached to the multiple bond, thus creating steric hindrance. Because of the fact that the quantity of evolved hydrogen bromide, and hence also the quantity of hydrocarbon which is reacting abnormally, also increases in that case where the radical which is creating steric hindrance is located at a negatively polarized carbon atom, it might be assumed, therefore, that steric hindrance (branching at the multiple bond) inhibits for the most part normal addition of halogens, which, therefore, favors bromination according to scheme (II).

EXPERIMENTAL

The hydrocarbons used were prepared synthetically by the Grignard reaction, with subsequent dehydration of the alcohols, and according to the Grignard-Wurtz reaction. The conditions of synthesis, and the constants for the resulting hydrocarbons, were published earlier by the author [8].

The solution for bromination was prepared by addition of 3 - 4 ml of bromine to 1 liter of methanol saturated with sodium bromide. By maintaining the above indicated conditions, the ratio of hydrogen bromide to

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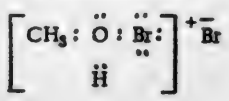

free bromine in the initial solution does not exceed 0.5-1 mol%. With prolonged storage of the solution, the amount of hydrobromic acid in it may increase somewhat (up to 2%), and accurate data therefore, upon analysis of the hydrocarbon mixtures, can be obtained only when the hydrobromic acid contained in the initial solution is taken into account.

The procedure for determination of hydrogen bromide formed by bromination of olefins is close to the procedure for determination of bromine numbers according to Kaufman [2].

A measured volume (0.1 - 0.5 ml) of the hydrocarbon to be investigated was added to 20 ml of bromine solution. After addition of 10% aqueous potassium iodide solution, and one-minute standing, the excess bromine was titrated with thiosulfate. After decolorization, 20ml of 5% potassium iodate was added to the flask, and the precipitated iodine filtered off a second time. Experimental data indicated that the hydrogen bromide formation reaction and the bromine addition proceed quite rapidly, and that one-minute standing of the hydrocarbon investigated in the bromine solution suffices.

Investigation of the bromination products was carried out by the author, using as an example, 2,5-dimethylhexene-2. The bromides resulted from slow addition of the hydrocarbon to 1 liter of bromine solution to the point of complete decolorization of the latter. The methanol solution of bromides obtained in this manner was diluted with water, and the bromides were then extracted with ether. After evaporation of the main ether volume (in an open beaker), the residue was dried with $CaCl_2$ and blown in vacuo (10 mm) with nitrogen for complete removal of the hydrocarbon, methanol and ether residues. Products resulting from these procedures were colorless and possessed the following properties:

n_D^{20} 1.4860; d_4^{20} 1.3300.

Found %: C 42.50, 42.38; H 7.06, 6.99; O 3.8, 4.2; Br 46.4, 46.6 (Carius); OCH_3 6 (Zeisel)

SUMMARY

1. Bromination of unsaturated hydrocarbons with a Kaufman solution has been investigated.

2. It has been shown that the amount of hydrogen bromide evolved in this case depends upon the structure of the olefins brominated, and increases in the following order: olefins with primary-secondary double bond < olefins with tertiary double bond < olefins with tertiary double bond and radicals creating steric hindrance.

3. A bromination scheme explaining the results has been proposed.

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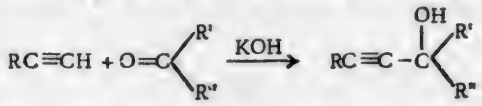
DERIVATIVES OF ACETYLENE. 160. CONDENSATION OF ALDEHYDES AND KETONES WITH ACETYLENE UNDER PRESSURE

A NEW PROCEDURE FOR SYNTHESIS OF ACETYLENIC ALCOHOLS

I. N. Nazarov, I. L. Kotlyarevsky and V. F. Ryabchenko

Of the described synthetic procedures for acetylenic alcohols, the simplest method is that of A. E. Favorsky [1], which consists of condensing acetylene with ketones under the influence of powdered potassium hydroxide:



With all of its advantages, however, this method has a number of significant disadvantages which limit its range of usefulness. In particular, the Favorsky method is inapplicable to the synthesis of secondary acetylenic alcohols by the condensation of acetylene with aldehydes [2, 3]. Directions for synthesis of secondary acetylenic alcohols, according to the Favorsky method, are to be found for the most part in the patent literature [4, 5, 6, 7], where conditions for reaction, and yields of secondary alcohols, are not given. Special attention is given in these works to solvents, for which role acetals, ethylene glycol esters and diethylene glycol, as well as hydrocarbons boiling above 100°, are proposed.

The most wide-spread synthetic procedure for secondary acetylenic alcohols is the method of Iotsich [8], which gives good alcohol yields, however, only when starting with monosubstituted acetylene, the method being based upon condensation of aldehydes with acetylenides of an alkali metal in liquid ammonia, which presents inconveniences associated with use of large quantities of liquid ammonia.

The great drawback of the latter procedure is its exceptional sensitivity to moisture, the presence of which lowers sharply the yields of acetylenic alcohols [9]. The method of synthesizing secondary acetylenic alcohols under the influence of sodamide and potassium hydroxide mixture [10], published in 1945, suffers from the same disadvantage.

Research carried out for several years in the authors' laboratory in the field of acetylenic alcohol reactions, made it necessary to develop a simple synthetic method for acetylenic alcohols which would excel in simplicity, in accurate reproducibility of results, and produce sufficiently high yields.

Having studied the Favorsky reaction, the authors concluded that it proceeds according to metalloorganic mechanism by formation of potassium acetylenide [11]. By studying its kinetics [12], Korotkov and Parfenova also arrived at the same conclusion regarding the mechanism for this reaction. The authors observed that the solubility of acetylene in ether increases markedly upon addition of potassium hydroxide to the ether. Considering this phenomenon to be associated with the formation of potassium acetylenide, the authors decided to investigate the Favorsky reaction course under acetylene pressure, assuming that the pressure would promote displacement of the $HC\equiv CH + KOH \rightleftharpoons HC\equiv CK + H_2O$ equilibrium in the direction of potassium acetylenide formation, and consequently to formation of conditions favorable to condensation of acetylene with carbonyl compounds. There is given in the literature only one brief patent direction for the Favorsky reaction carried out under pressure [13], and there attention is paid to this simply to decrease condensation of acetone itself under the influence of potassium hydroxide.

The authors method for carrying out the Favorsky reaction consists of the following: pulverized potassium hydroxide is charged into a metallic reactor (see below), along with ether dried over calcium chloride. The mixture is saturated with acetylene under 5 - 10 atmospheres, with vigorous stirring, the pressure being maintained during the entire course of reaction. Aldehyde or ketone is then added at a uniform rate from a dropping funnel, working under pressure, into the reactor, with vigorous stirring. Stirring is continued for an additional 20-30 minutes, after which pressure is released and the reaction mixture treated with water taken in equal or double amount according to the weight of alkali. The product is then neutralized with carbon dioxide, extracted with

ether, dried with potash and fractionated. The crude acetylenic alcohol, after the first fractionation, was dried with potash and fractionated on a column with 25 theoretical plates, whose effectiveness was measured at the height of irrigation.

Working in accordance with this method, the secondary and tertiary acetylenic alcohols given in the Table were obtained.

Expt. No.	Aldehyde or ketone	Acetylenic alcohol	Yield of pure alcohol (%)	
			Without presence of aliphatic alcohols	In the presence of aliphatic alcohols
1	Acetaldehyde	1-Butyn-3-ol	20	43
2	Propionic aldehyde	1-Pentyn-3-ol	36	45
3	n-Butyric aldehyde	1-Hexyn-3-ol	51.5	59
4	Iso-butyric aldehyde	4-Methyl-1-pentyn-3-ol	47.5	50
5	Hydrocinnamic aldehyde	5-Phenyl-1-pentyn-3-ol	37.7	54.5
6	Enanthol	1-Nonyn-3-ol	51.5	–
7	Isovaleric aldehyde	5-Methyl-1-hexyn-3-ol	74.5	–
8	Acetone	3-Methyl-1-butyn-3-ol	93	–
9	Methylethyl ketone	3-Methyl-1-pentyn-3-ol	80	–
10	Diethyl ketone	3-Ethyl-1-pentyn 3-ol	82	–
11	Di-n-propyl ketone	3-Propyl-1-hexyn-3-ol	70	–
12	Isobutyrone	3-Isopropyl-4-methyl-1-pentyn-3-ol	–	65
13	Cyclohexanone	1-Ethynyl-1-cyclohexanol	96.7	–
14	Cyclopentanone	1-Ethynyl-1-cyclopentanol	–	42
15	Acetophenone	3-Phenyl-1-butyn-3-ol	–	70
16	Mesityl oxide	3,5-Dimethyl-4-hexen-1-yn-3-ol	–	5.2

With further study, it was found that the yield of acetylenic alcohols increases considerably with a mixture of potassium hydroxide and ether containing a small amount of aliphatic alcohols, the most effective among which were found to be ethanol and n-butanol. The yield of acetylenic alcohols obtained by condensation of aldehydes and ketones with acetylene under pressure in the presence of small additions of ethanol or of n-butanol are given in the last column of the Table.

The procedure described makes it possible also to effect condensation of acetylene with cyclopentanone, acetophenone and mesityl oxide, which were heretofore, impossible to combine. An attempt to condense carbon dioxide with acetylene by this procedure gave only traces of propiolic acid. Negative results were obtained when attempting to condense acetylene with paraform, acrolein and benzaldehyde.

EXPERIMENTAL

Description of the Reactor for Condensing Aldehydes and Ketones Under Pressure

Condensation of aldehydes and ketones with acetylene under pressure was carried out in a steel reactor of 1 liter volume, tested for 50 atmospheres, equipped with a jacket for water or brine cooling and with a propeller stirrer for 500 - 1000 revolutions/ minute. The body of the reactor had a flat collar with a lead sealer. Bolts were threaded into the collar to fasten down the lid which contained two special doors for charging reactants, a tripod and manometer, greasing stick for lubricating the stirrer gasket, two gas inlet tubes and one gas outlet tube for reducing pressure. A connecting pipe screwed into a sleeve was connected to the bottom of the reactor. Such an arrangement permitted charging and discharging without removing the lid. The reactor had a steel dropping funnel of 200 ml volume, through which was fed by liquid pump into the reactor at a uniform rate either aldehyde or ketone, and acetylene entered the reactor at a given pressure via the gas connecting tube.

Description of the Synthetic Method for Acetylenic Alcohols, Using Pressure

Dry ether was charged into the above-described steel reactor, powdered potassium hydroxide, and if needed, a small amount of alcohol added. The air was displaced from the reactor by nitrogen, using two washings with the

gas under 5-8 atmospheres pressure. With the stirrer going, the mixture was saturated with acetylene at a given temperature (0-20°) and a given pressure (5-10 atm). after which either aldehyde or ketone was fed through the dropping funnel into the reactor at a uniform rate (over a period of 0.5-1 hour). The given pressure in the reactor (5-10 atm). was maintained during the entire experiment, readily maintained by regulating the feed rate of carbonyl compound and acetylene. Following addition of all aldehyde or ketone, the reaction mixture was stirred for another 30-40 minutes, treated with water (equal or double quantity according to the weight of alkali), the product neutralized with carbon dioxide, extracted with ether, dried with potash, and fractionated. After distilling off the ether, the acetylenic alcohol was first distilled in the usual manner, and then on a column with 25 theoretical plates. If necessary, the acetylenic alcohol after the first distillation, was again dried with potash.

Pressure greatly accelerated condensation of acetylene with aldehydes and ketones, and made it possible to effect... this reactioh within a short space of time (1-2 hours). There was also eliminated side formation of glycols, which increased considerably the yield of acetylenic alcohols, reaching almost theoretical values in the case of aliphatic and alicyclic ketones For condensation of ketones with acetylene, a pressure of 5 atm. was quite sufficient, while condensation of aldehydes with acetylene was carried out at 8-10 atmospheres of pressure. Better yields of acetylenic alcohols from condensation of ketones with acetylene were obtained at a temperature of 15-20°, and for condensation of aldehydes with acetylene, it was better to carry out reaction at a temperature of 0°, or even −5°. Of real importance is good stirring of the reaction mixture, which becomes very viscous at the end of the experiment. In the reactor described, of 1 liter volume, stirring at 900-1000 r.p.m. was used, and for a reactor on larger scale (6 liters), stirring at 400-500 r. p. m. was found satisfactory. Ethers, acetals or hydrocarbons could be used as solvents for condensation of aldehydes and ketones.

Condensation of Acetylene with Acetaldehyde. a) A mixture of 65 g powdered potassium hydroxide and 250 ml of dry ether was saturated with acetylene at 0° and 10 atm. pressure. 28 g of acetaldehyde (b.p. 21-23°) was introduced into the reactor over a period of 50 minutes, with vigorous stirring; the mixture was stirred for another 20 minutes at 0° and 10 atm. pressure. The product was processed as described above and fractionated on a column. 9 g of 1-butyn-3-ol with b.p. 107-108° resulted: n_D^{23} 1.4250 [14]. Yield 20.2 %.

b) A mixture of 64 g of potassium hydroxide, 250 ml of ether (dry) and 3 ml of ethanol (95 %) was saturated with acetylene at 0° and 10 atm. pressure. 44 g of acetaldehyde (b.p. 21-22°) was introduced into the reactor over a period of 33 minutes, and the reaction mixture stirred for another 20 minutes, and treated in the usual fashion. 30 g of pure 1-butyn-3-ol with b.p. 107-108° resulted; n_D^{20} 1.4250. Yield was 43 %.

Condensation of Acetylene with Propionic Aldehyde. a) A mixture of 60 g of powdered potassium hydroxide and 300 ml of ether was saturated with acetylene at 0°, and a pressure of 8 atm. 29 g of propionic aldehyde (b.p. 47-49°) was introduced into the reactor over a period of 90 minutes. Stirring at 0° and at a pressure of 8 atm. was continued for another 30 minutes. After processing, 15 g of pure 1-pentyn-3-ol, with b.p. 124° resulted; n_D^{20} 1.4332 [15]. Yield 36 %.

b) A mixture of 64 g potassium hydroxide, 250 ml of dry ether and 5 ml of ethanol (95 %) was saturated with acetylene at 0° and 8.8 atm. pressure. 58 g of propionic aldehyde (b.p. 47-49°) was introduced into the reactor with vigorous stirring over a period of 30 minutes. The reaction mixture was then stirred for another 20 minutes. 38 g of pure 1-pentyn 3-ol with b.p. 124° resulted; n_D^{20} 1.4332. Yield 45.2 %.

Condensation of Acetylene with n-Butyric Aldehyde. 50 g of powdered potassium hydroxide and 250 ml of ether were saturated with acetylene at 0° and 10 atm. pressure. Within a period of 60 minutes, 32 g of n-butyric aldehyde (b.p. 74-76°) was introduced into the same apparatus. After stirring for another half-hour, followed by the usual treatment of product, 22 g of pure 1-hexyn-3-ol with b.p. 143.5°, resulted; n_D^{20} 1.4350 [15]. Yield was 51.5 %.

Condensation of Acetylene with Isobutyric Aldehyde. 80 g of powdered potassium hydroxide and 350 ml of ether were saturated with acetylene at 0° and a pressure of 8.6 atmospheres. 53 g of isobutyric aldehyde (b.p. 63-64°) was introduced into the reactor over a period of 70 minutes. 33 g of 4-methyl-1-pentyn-3-ol with b.p. 133° resulted; n_D^{20} 1.4353 [16]. Yield was 47.5 %.

Condensation of Acetylene with Hydrocinnamic Aldehyde. a) 40 g of the hydrocinnamic aldehyde was added to a mixture of 50 g of powdered potassium hydroxide and 250 ml of ether saturated with acetylene at 0° and a pressure of 8.4 atm.; over a period of 85 mintues, stirring then continued for another 30 minutes. After the usual treatment and distillation in vacuo, 18.5 g of pure 5-phenyl-1-pentyn-3-ol with b.p. 125-125.7° at 10 mm was isolated; n_D^{20} 1.5350. Yield 37.7 %.

b) 40 g of hydrocinnamic aldehyde was added over a period of 55 minutes to a mixture of 50 g of potassium hydroxide, 250 ml of dry ether, and 1.5 ml of ethanol (95%) saturated with acetylene at 0° and a pressure of 3.5 atm. After 30 minutes stirring, the product was treated as usual and fractionated in vacuo. 26 g of pure 5-phenyl-1-pentyn-3-ol with b.p. 125-126° at 10 mm was isolated; n_D^{20} 1.5350. Yield was 54.5%.

Condensation of Acetylene with Isovaleric Aldehyde. 48 g of powdered potassium hydroxide and 250 ml of ether were saturated with acetylene at 0° and 10 atm. pressure. 32 g of isovaleric aldehyde (b.p. 90-92°) was introduced into the apparatus over a period of 75 minutes. Stirring was continued for another 25 minutes. After the usual processing, followed by fractionation on a column, 31 g of 5-methy-1-hexyn-3-ol with b.p. 154-154.4°, resulted; n_D^{20} 1.4378. Yield was 74.5%.

Condensation of Acetylene with Enanthol. A mixture of 30 g powdered potassium hydroxide and 200 ml of ether was saturated with acetylene at 0° and 8 atm. pressure. 23 g of enanthol was introduced into the reactor over a period of 1 hour. Stirring was continued for another 30 minutes. 14.5 g of 1-nonyn-3-ol with b.p. 89-91° at 12 mm was isolated: n_D^{20} 1.4444 [17].

Condensation of Acetylene with Acetone. 60 g of powdered potassium hydroxide and 180 ml of ether were saturated with acetylene at 0° and 7 atm.. pressure. 29 g of acetone was introduced into the receiver over a period of 30 minutes. Stirring was continued for another 30 minutes. After the usual treatment and fractionation on a column, 39 g of dimethylethynylcarbinol resulted with b.p. 103.5°; n_D^{20} 1.4211. Yield was 93%.

Condensation of Acetylene with Methylethyl ketone. A mixture of 65 g of powdered potassium hydroxide and 250 ml of ether was saturated with acetylene at 20° and 7 atm. pressure. 36 g of methylethyl ketone (b.p. 76 - 78°) was introduced into the reactor over a period of 45 minutes. Stirring was continued for another 30 minutes. After the usual treatment, and fractionation on a column, 39.2 g of 3-methyl-1-pentyn-3-ol with b.p. 121.5° was isolated; n_D^{20} 1.4309 [18, 19].

Condensation of Acetylene with Diethyl ketone. 42 g of powdered potassium hydroxide and 250 ml of ether. at 0° and 7.6 atm. were saturated with acetylene. 30 g of diethyl ketone was introduced into the reaction mixture over a period of 100 minutes. After treatment and distillation on a column, 32 g of 3-ethyl-1-pentyn-3-ol with b.p. 137-138.4° was isolated. n_D^{20} 1.4364 [20, 21]. Yield was 92%.

Condensation of Acetylene with Di-n-propyl Ketone. 31 g of powdered potassium hydroxide and 50 ml of ether were saturated with acetylene at 0° and 7.2 atm. pressure. 29 g of di-n-propyl ketone was introduced into the reactor over a period of 80 minutes. Stirring was continued for another 30 minutes. After usual treatment and distillation on the column, 25 g of 3-propyl-1-hexyn-3-ol with b.p. 173-174° was isolated; n_D^{20} 1.4375 [22].

Condensation of Acetylene with Isobutyrone. 65 g of powdered potassium hydroxide, 250 ml of ether and 5 ml of ethanol (95%) were saturated with acetylene at 0° and 7.6 atmospheres pressure. 114 g of isobutyrone (b.p. 120 - 124°) was introduced into the reactor over a period of 40 minutes. Stirring was continued for another 15 minutes. After the usual treatment and fractionation on a column, 91 g of 4-methyl-3-isopropyl-1-pentyn-3-ol with b.p. 165.5° was isolated; n_D^{20} 1.4500 [21]. Yield was 65%.

Condensation of Acetylene with Cyclopentanone. 42 g of powdered potassium hydroxide, 200 ml of ether, and 3 ml of ethanol were saturated with acetylene at 0° and 8 atm. pressure. 52 g of cyclopentanone was introduced into the receiver over a period of 20 minutes. Stirring after introduction of the ketone was continued for another 15 minutes. After the usual treatment and fractionation on a column, 28 g of 1-ethynyl-1-cyclopentanol with b.p. 157° was isolated, m.p. 27° [23].

Condensation of Acetylene with Cyclohexanone. A mixture of 40 g of powdered potassium hydroxide and 250 ml of ether was saturated with acetylene at 0° and 7.6 atm. pressure. 29 g of cyclohexanone (b.p. 155°) was introduced into the receiver over a period of 75 minutes. Stirring was continued for another 30 minutes. After the usual treatment, 35.5 g of 1-ethynyl-1-cyclohexanol with b.p. 179° was isolated; m.p. 31-32° (from petroleum ether) [22, 23, 24]. Yield was 96.7%.

Condensation of Acetylene with Acetophenone. 65 g of powdered potassium hydroxide 250 ml of ether and 5 ml of ethanol were saturated with acetylene at 0° and 10 atm. pressure. 120 g of acetophenone was added to the reactor over a period of 45 minutes. After the usual treatment, 100 g of acetophenone was recovered and 17 g of 3-phenyl-1-butyn-3-ol, b.p. 82-83° at 4 mm; m.p. 49° [24, 25]. Yield was 11.6%, calculating on the basis of acetophenone taken for reaction, and on the basis of acetophenone reacted was 70%.

Condensation of Acetylene with Mesityl Oxide. 33 g of powdered potassium hydroxide, 250 ml of ether and 2.5 ml of ethanol were saturated with acetylene at 0° and 10 atm. pressure. 50 g of mesityl oxide was introduced into the reactor over a period of 35 minutes. Stirring was continued for another 30 minutes. After the usual treatment, 23 g of mesityl oxide was isolated and 2 g of pure 3,5-dimethyl-4-hexen-1-yn-3-ol with b.p. 65-66° at 17 mm; n_D^{20} 1.4629. The yield was 2.5% calculating on the basis of ketone introduced into reaction, and 5.2% on the basis of ketone reacted.

SUMMARY

A new method for condensing aldehydes and ketones with acetylene under pressure has been developed, which permits rapid synthesis of secondary and tertiary acetylenic alcohols in good yield.

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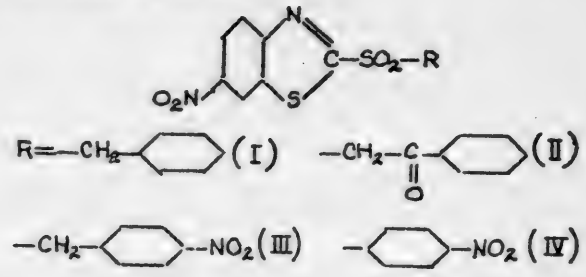
HYDROLYTIC RUPTURE OF BENZTHIAZOLYL-2-ARYL- AND ALKYLSULFONES

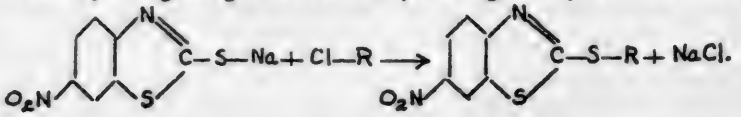
1. REACTION MECHANISM FOR RUPTURE OF 6-NITRO-BENZTHIAZOLYL-2-ARYL- AND ALKYLSULFONES

I. Ya. Postovsky and I. A. Alekseeva

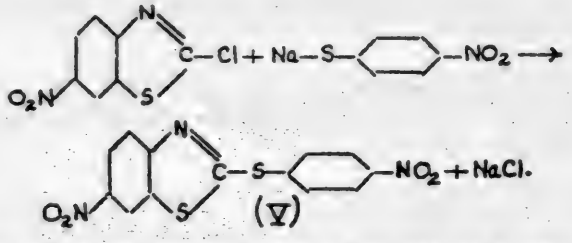
In studying certain benzthiazole (I - IV, VIII) sulfones, their instability relative to dilute acids and alkalies was observed. Under the influence of these substances, sulfones of the benzthiazole series undergo hydrolytic rupture, from which reaction products 6-nitro-2-benzthiazolone readily separates. This characteristic case of hydrolytic rupture of the sulfones is of decided theoretical interest, a fact which prompted the authors to engage in the task of clarifying the mechanism of this new type of rupture.



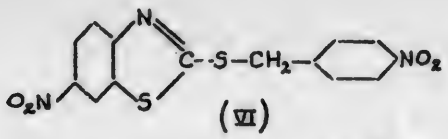
Sulfones result from oxidation of sulfides by potassium permanganate or hydrogen peroxide in acetic acid solution. The sulfides required for this purpose were synthesized by condensing the sodium salt of 2-mercapto-6-nitrobenzthiazole with the corresponding halogen derivative, by heating in ethyl alcohol with KI addition:



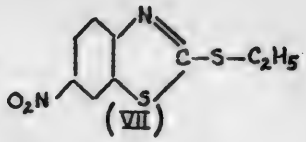
Synthesis of p-nitrophenylsulfide (V) was not accomplished in similar fashion because of the relatively low reactivity of the halogen in the p-nitrochlorobenzene. Sulfide (V) resulted in good yield on condensing 2-chloro-6-nitrobenzthiazole with the sodium salt of p-nitrothiophenol:



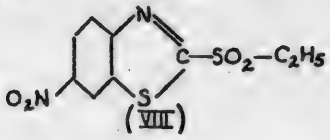
In approaching a study of the mechanism of rupture of sulfones in the benzthiazole series, it was necessary to clarify first of all whether or not hydrolytic rupture is characteristic only for sulfones, or whether similar corresponding sulfides of the benzthiazole series are not also subject to similar rupture. It was found that sulfides are not capable of hydrolytic rupture under those conditions wherein the sulfones rupture with relative facility upon reaction with aqueous solutions of acids and alkalies. This fact was established by studying the hydrolysis reaction of compound (III), and the corresponding initial sulfide (VI), as well as compounds (VII) and (VIII) with aliphatic radicals:



(VI)



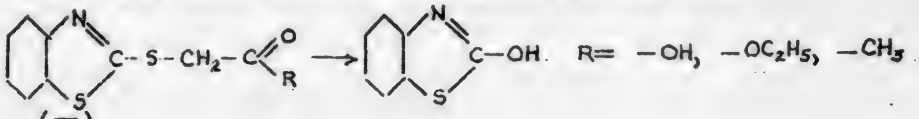
(VII)



(VIII)

Thus, for example, sulfide (VI) did not change noticeably with 2 hours heating in 2N NaOH at 94°. However, under these conditions, the corresponding sulfone (III) was ruptured about 85%. Sulfide (VII) was hardly ruptured either by 1 hour heating with 2N NaOH at 94°, or by 1 hour heating with dilute hydrochloric acid at the same temperature, while at the same time sulfone (VIII) hydrolyzed smoothly under these conditions.

Hydrolytic rupture of sulfones of the benzthiazole series has not been described in the literature up to date. Only V. F. Kucherov [1] reported that oxidation of type (IX) sulfides with hydrogen peroxide at 60 - 70° in glacial acetic acid medium proceeds differently than oxidation of simple alkylbenzthiazolyl-2-sulfides, and does not lead to production of the corresponding sulfones, but instead, to formation of benzthiazolone:



(IX)

In the authors' opinion there apparently occurs in this case a rupture of the corresponding sulfone by oxidation, and not rupture of the C—S bond of the sulfide or sulfoxide.

The rupture of sulfones is thought to be possible according to one of four routes, as the result of an attack by the hydrolyzing agent (water) on two sides of the sulfo bonds (at the C—SO_2 and at the SO_2—R bonds), (see scheme).

From the given schemes for possible rupture reactions, it can be seen that if rupture follows along the lines of 1 or 2, that one of the final products should then be 6-nitrobenzthiazole; according to route 1, it forms directly, and according to 2, via the intermediate product — the unstable sulfinic acid — which decomposes with sulfur dioxide evolution and production of 6-nitrobenzthiazole.•

According to routes 3 and 4, there should be formed upon hydrolysis the 6-nitro-2-hydroxybenzthiazole (6-nitrobenzthiazolone-2), whereas by route 4, it would result via the stage of the corresponding sulfo acid, which, when boiled, decomposes, forming 6-nitrobenzthiazolone-2.••

Below are results of the hydrolytic rupture of some derivatives of 6-nitrosulfone.

1) Hydrolysis of 6-nitrobenzthiazolyl-2-benzylsulfone (I). Hydrolysis was carried out by heating the product in 2N NaOH. Upon acidification of the hydrolyzate, 6-nitrobenzthiazolone-2 in a yield about 90% theory was isolated; the other part of the ruptured molecule could not be identified.

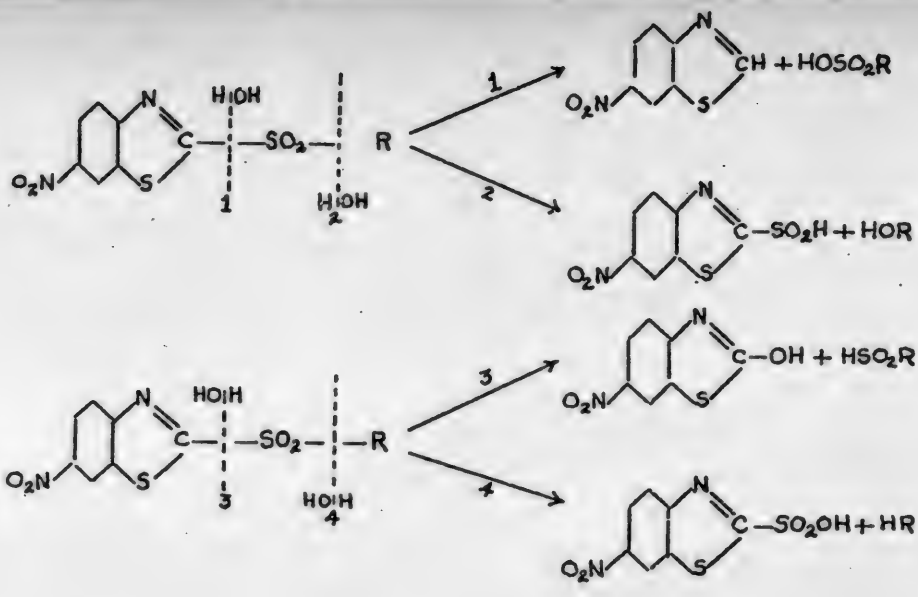
2) Hydrolysis of 6-nitrobenzthiazolyl-2-phenacetylsulfone (II). Upon heating in alkaline as well as acid medium, 6-nitrobenzthiazolone-2 in 96% yield, and acetophenone in 60% yield resulted (the latter being isolated from the hydrolyzate in the form of its semicarbazone). Consequently, the following reaction took place: [see(A) on next page].

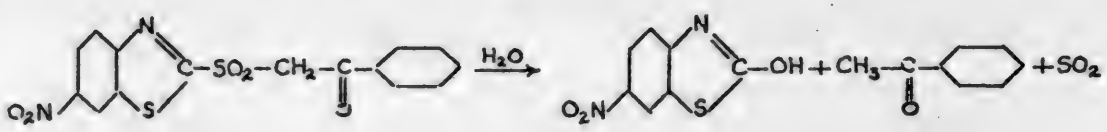
3) Hydrolysis of 6-nitrobenzthiazolyl-2-(4'-nitrobenzyl)sulfone (III). After boiling with 2N NaOH, 6-nitrobenzthiazolone-2 in 85% yield and p-nitrotoluene in approximately 52% yield of theory, were isolated and identified. Consequently, the hydrolysis in this case proceeded according to the scheme: [see (B) on next page].

In none of the given cases was it possible to isolate 6-nitrobenzthiazole, but each time the 6-nitrobenz-

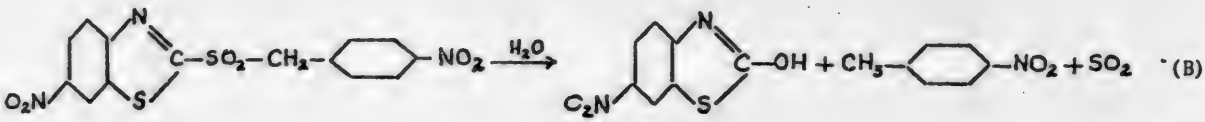
• Compare a similar reaction for benzthiazole-2-sulfinic acid [2].

•• See rupture reaction for benzthiazol-2-sulfo acid [3].





(A)

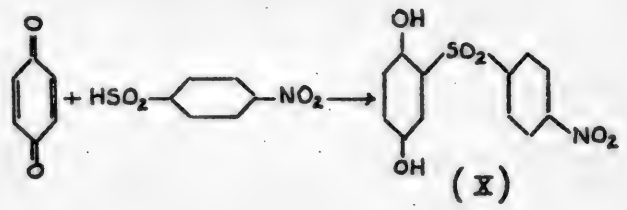


(B)

thiazolone-2 resulted in good yield. These data signify that rupture proceeds along routes 3 or 4. As yet, however, it has not been possible to decide on the basis of experimental data between 3 and 4, since the SO_2 could have been split off either from the benzthiazole sulfo acid or from the sulfinic acid, $R-SO_2H$.

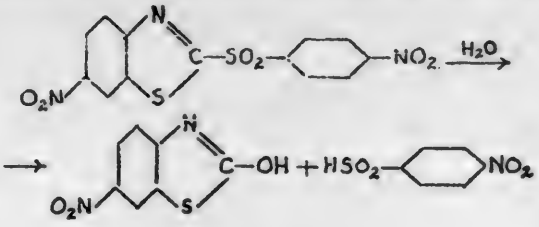
4) In the case of 6-nitrobenzthiazolyl-2-(4'-nitrophenyl)-sulfone (IV) hydrolysis it was possible to clarify the problem. In this experiment, p-nitrobenzenesulfinic acid was also isolated from the hydrolyzate of this experiment in addition to 6-nitrobenzthiazolone-2. The former is known to be a relatively stable compound. In fact, it was possible to prove the presence of this sulfinic acid in the mother liquor from the benzthiazolone, by adding p-quinone [4], whereupon 2,5-dihydroxy-4'-nitrodiphenylsulfone (X) resulted: [see (C) below).

This new compound was found to be identical with the sulfone synthesized from p-quinone and p-nitrobenzenesulfinic acid.



(X)

The results of the previous experiment indicated that hydrolytic rupture of compound (IV) proceeds along route 3.



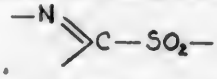
It is believed that hydrolytic rupture of other sulfones also proceeds according to this scheme.

Apparently, in those cases where unstable sulfinic acids result, as for example in the case of the rupture of sulfones (II) and (III), decomposition of the acid proceeds with sulfur dioxide evolution, forming the RH hydrocarbon. Upon hydrolysis of the sulfone (I), unstable benzylsulfinic acid is evidently formed; according to the literature data [5], the acid decomposes to dibenzylsulfoxide, benzaldehyde and sulfur dioxide, being partially oxidized by the air to benzylsulfo acid.

Hydrolytic rupture described in the present work occurs with the analogous benzthiazole compounds which do not contain the nitro group.

It has been stated above that benzthiazole sulfides do not rupture under those conditions whereby sulfones rupture readily, i.e., the C–S bond in sulfides is stronger than that in the sulfones.•

Such a peculiarity of the $C-SO_2$ bond is a result of mutual effect of the group in the benzthiazole sulfone molecule which has a characteristic sulfoazo methine grouping.



It might be assumed that the presence of this grouping in isosteric compounds would create a possibility for similar hydrolytic rupture.

Preliminary experiments were carried out by the authors on hydrolysis of 2-quinolyl-4'-nitrophenylsulfone. The results obtained (quinolone-2) speak in favor of the assumption proposed, which is in accord with the phenomenon discovered.

EXPERIMENTAL

I. Synthesis of Sulfides and Sulfones

1) 6-Nitrobenzthiazolyl-2-(benzyl)-sulfide: yellow needles, m.p. 114° (from alcohol), 114° indicated in the literature [6].

6-Nitrobenzthiazolyl-2-(benzyl)-sulfone (I), slightly-yellow needles with m.p. 192° (194° in the literature) [6].

2) 6-Nitrobenzthiazolyl-2-phenacetylsulfide. 21.2 g (0.1 mole) of 6-nitro-2-mercaptobenzthiazole was dissolved in a mixture of 200 ml. ethyl alcohol and 50 ml. of 2N NaOH. An alcoholic solution of 11.7 g (0.1 mole) of chloroacetophenone (m.p. 58 - 59°) was added to the hot solution of the sodium salt of potassium iodide, 16 g (0.1 mole). A yellow substance precipitated immediately. The reaction mass was boiled for 1 hour, poured into ice water, and the yellow needle precipitate filtered off. After double recrystallization from dilute alcohol, yellow needles with a constant m.p. of 129-130°, precipitated. Yield was 21 g (60%). The sulfide was readily soluble in methyl, ethyl and butyl alcohols, by heating, poorly so in benzene, and glacial acetic acid.

3.595 mg substance: 0.270 ml N_2 (24°, 745 mm). Found %: N 8.45. $C_{15}H_{10}O_3N_2S_2$. Calculated %: N 8.48.

3) 6-Nitrobenzthiazolyl-2-(phenacetyl)-sulfone (II). A 7.5% solution of potassium permanganate was added to a solution of 21 g of sulfide in 1.0 liter of glacial acetic acid, to a constant raspberry red coloration.

• Evidently the distance between the carbon atom and the sulfur atom in the sulfones (I–IV, VIII) is greater than the distance between these atoms in the corresponding sulfides (it would be interesting to verify this assumption by X-ray analysis).

The excess potassium permanganate was then tied up with sodium bisulfite solution. Sulfone needles precipitated out from the solution diluted with water; after double recrystallization from dilute acetone, the m.p. was 173-174°. Yield was 5 g (25%). The sulfone was readily soluble in the cold with respect to acetone and in hot butyl alcohol.

3.270 mg substance: 0.235 ml N_2 (25°, 745 mm). Found %: N 8.07. $C_{15}H_{10}O_5N_2S_2$. Calculated %: N 7.73.

4) 6-Nitrobenzthiazolyl-2-(4'-nitrobenzyl)-sulfide. 0.1 mole (17.2 g) of p-nitrobenzyl chloride (m.p. 71°) and 16 g (0.1 mole) of KI were added to 21.2 g (0.1 mole) of 6-nitro-2-mercaptobenzthiazole in solution with 200 ml of alcohol. The resulting mixture was boiled for 2 hours, and poured into ice water. After recrystallization from nitrobenzene, there resulted 30 g of sulfide (88%) in the form of yellow needles with m.p. 181°. The sulfide was poorly soluble in ethyl alcohol and acetone, more readily in butyl alcohol.

3.925 mg substance: 0.431 ml N_2 (21°, 743 mm). 28.55 mg substance: 37.5 mg $BaSO_4$. Found %: N 12.46; S 18.04. $C_{14}H_9O_4N_3S_2$. Calculated %: N 12.12; S 18.46.

5) 6-Nitrobenzthiazolyl-2-(4'-nitrobenzyl)sulfone (III). 7 g (0.02 mole) of sulfide and 750 ml of glacial acetic acid were oxidized with 7.5% potassium permanganate. The reaction product was recrystallized from a large volume of acetone, and came out in the form of silky needles with m.p. 227-228°. Yield of sulfone was 6.5 g (85%). The sulfone was poorly soluble in boiling acetone and alcohol, but readily soluble in hot nitrobenzene, and insoluble in water.

4.075 mg substance: 0.416 ml N_2 (21°, 741 mm). 32.70 mg substance: 39.6 mg $BaSO_4$. Found %: N 11.57; S 16.60. $C_{14}H_9O_6N_3S_2$. Calculated %: N 11.07; S 16.90.

6) 6-Nitrobenzthiazolyl-2-(4'-nitrophenyl)-sulfide. 9 g of 2-chloro-6-nitrobenzthiazole (0.042 mole) was dissolved with heating in 500 ml of ethyl alcohol. 3.2 g NaOH was added to a hot solution of the sodium salt of p-nitrothiophenol (9 g of thiophenol in an alcoholic solution). A yellow-gray substance precipitated. The yield was 10.4 g (80%).

9.5 g of sulfide resulted as yellowish needles with m.p. 174-175° upon recrystallization from glacial acetic acid.

5.800 mg substance: 0.622 ml N_2 (19°, 749 mm). Found %: N 12.35. $C_{13}H_7O_4N_3S_2$. Calculated %: N 12.61.

7) 6-Nitrobenzthiazolyl-2-(4'-nitrophenyl)-sulfone (IV). 10.5 g (0.03 mole) of the sulfide was dissolved with heating in 500 ml of glacial acetic acid. The cooled sulfide acetate solution was oxidized with 7.5% permanganate solution. The resulting sulfone was recrystallized from a large volume of boiling acetone. Colorless, silky needles with m.p. 274-275°, yield 10.1 g, which amounted to about 84% of theory. The sulfone was poorly soluble in alcohol and acetone, glacial acetic acid and benzene.

4.700 mg substance: 0.460 ml N_2 (17°, 744 mm). Found %: N 11.27. $C_{13}H_7O_6N_3S_2$. Calculated %: N 11.50.

II. Hydrolytic Rupture of Sulfones.

1) Rupture of 6-Nitrobenzthiazolyl-2-(benzyl)-sulfone (I) a) Alkaline rupture. A suspension of 3.5 g (0.01 mole) of sulfone in 300 ml of 2N NaOH was heated in a round-bottomed flask equipped with reflux condenser. A dark-brown solution gradually formed, with an odor of benzaldehyde. The alkaline solution was neutralized with dilute hydrochloric acid. The substance which precipitated was filtered off. The resulting product had an m.p. of 249-250°. A sample mixed with known 6-nitrobenzthiazolone-2 did not give depression in melting point. The yield of 6-nitrobenzthiazolone-2 was 2.1 g (91%).

b) Acid rupture. The acid rupture was carried out in a dilute hydrochloric acid medium (1:1). The acid hydrolyzate was made alkaline with concentrated alkali to a definite alkaline reaction. The results obtained were analogous to the results in the sulfone rupture experiments in alkaline medium. 3.6 g of 6-nitrobenzthiazolone-2 was isolated from 6.5 g of sulfone after hydrolysis, which amounted to 92% of theory.

2) Rupture of 6-Nitrobenzthiazolyl-2-(phenacetyl)-sulfone (II). a) Alkaline rupture. 0.1 g of sulfone (m.p. 173-174°) was placed in a round-bottomed flask equipped with reflux condenser. 5 ml of 2N—NaOH was poured into the flask. Already at room temperature rupture began, evident by gradual fading of the sulfone precipitate, and the formation of a dark-brown solution with strong acetophenone odor. The sulfone ruptured completed at 60° within 5 minutes.

The solution was extracted with ether. After distilling off the ether, there was a little liquid in the residue with strong acetophenone odor. Acetophenone was identified by its semicarbazone, obtained by addition of semicarbazide and sodium acetate to the liquid under investigation, with subsequent boiling of the mixture. The resulting product (0.03 g) had an m.p. of 199-200°. A sample mixed with known semicarbazone of acetophenone (m.p. 203°) did not give depression. The yield of acetophenone was approximately 60% of theory.

The alkaline solution was acidified with 50% acetic acid, whereupon 6-nitrobenzthiazolone-2 precipitated in the amount of 0.052 g (96%).

b) Acid rupture. Upon acid rupture, 6-nitrobenzthiazolone-2 and acetophenone (identified in the form of its semicarbazone) were isolated from the hydrolyzate.

3) Rupture of 6-Nitrobenzthiazolyl-2-(4'-nitrobenzyl)-sulfone (III). 6.4 g (0.02 mole) of sulfone (m.p. 181°) was heated with 2N NaOH (400 ml) in a round-bottomed flask equipped with reflux condenser. The precipitate dissolved gradually and the solution became dark-brown in color. Boiling was continued for approximately 2 hours. p-Nitrotoluene was distilled off from the alkaline solution with steam. The product isolated had an m.p. of 55°. A sample mixed with p-nitrotoluene melted without depression. Yield was 1.2 g (52%).

The alkaline solution which was filtered off was treated with 50% acetic acid to a weakly acid reaction to litmus. From this solution there precipitated a dark-yellow substance with m.p. 247-250°. The product, which was purified by recrystallization from alcohol with added activated charcoal, was in the form of colorless needles with m.p. 249-250°. The yield was 2.8 g (35%). The product was identified as 6-nitrobenzthiazolone by the melting point of a mixed sample.

4) Rupture of 6-Nitrobenzthiazolyl-2-(4'-nitrophenyl)-sulfone (IV). 0.2 g of sulfone was boiled for 0.5 hour with 40 ml of 2N NaOH in a flask equipped with reflux condenser. The solution gradually acquired a dark-brown color, and there settled to the bottom of the flask a precipitate of the sodium salt of 6-nitro-2-hydroxybenzthiazole. The precipitate was filtered off and dissolved in water. Upon acidification of the resulting solution with hydrochloric acid, there was formed a precipitate with m.p. 248-249°. There was no depression when melted with known 6-nitrobenzthiazolone-2. From the dark-brown filtrate of the sodium salt, the addition of dilute hydrochloric acid (1:1) precipitated out some more 6-nitrobenzthiazolone-2.

0.03 g of finely-powdered p-quinone was added to the hydrochloride filtrate. An amorphous precipitate formed upon gentle heating, which was filtered off. Recrystallized from dilute alcohol, the product had an m.p. of 208-209°. The resulting product had all the properties of 2,5-dihydroxy-4'-nitrodiphenylsulfone. A sample mixed with the known, synthesized for this purpose, 2,5-dihydroxy-4'-nitrodiphenylsulfone, did not give depression.

5) Synthesis of 2,5-Dihydroxy-4'-nitrodiphenylsulfone. 0.25 g of p-nitrobenzylsulfinic acid (prepared from p-nitrophenylsulfochloride by reduction with sodium sulfite [7]) was dissolved, with gentle heating, in 10 ml of water. The calculated quantity of powdered p-quinone (0.08 g) was added to the solution cooled to room temperature. Slightly yellow flakes immediately precipitated out at room temperature at the same time that the yellow crystalline precipitate of turbid quinone disappeared. The precipitate of resulting sulfone was filtered off and recrystallized from 30% alcohol. Needles with m.p. 210-211° resulted. The product was readily soluble at room temperature in alkali, forming a red-brown solution.

3.410 mg substance: 0.152 ml N_2 (25°, 738 mm). Found %: N 4.96. $C_{12}H_9O_5NS$. Calculated %: N 4.72.

SUMMARY

1. It has been demonstrated that 6-nitrobenzthiazolyl-2-arylsulfones and alkylsulfones in alkaline and in acid solution are subject to hydrolytic rupture, with formation of 6-nitrobenzthiazolone-2.

2. The reaction mechanism for hydrolytic rupture of sulfones has been studied.

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INTERACTION OF METHYLENE HETEROCYCLIC NITROGEN BASES WITH QUINONES

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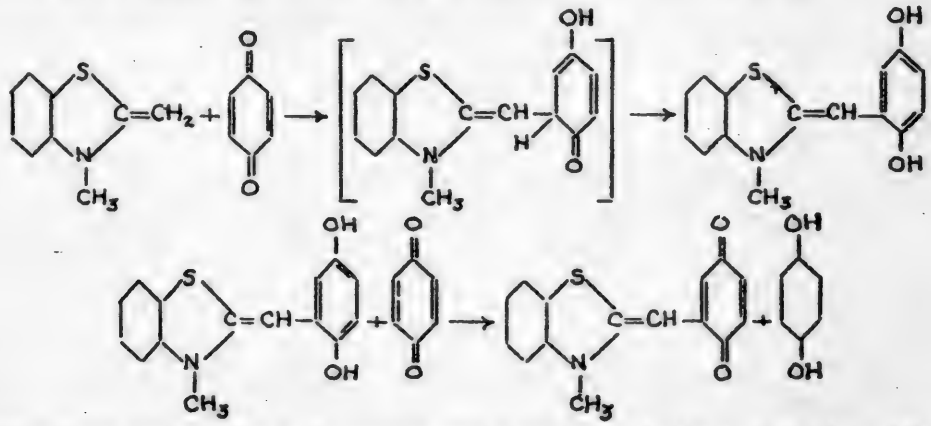
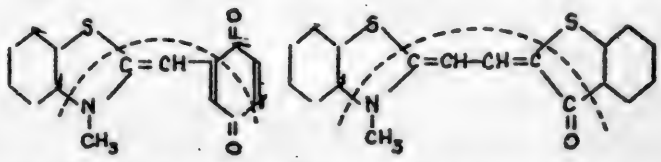
Several examples of condensation between quinones and methylene heterocyclic nitrogen bases are known. In 1937, the reaction of 2,3-dichloro-1,4-naphthoquinone with quinaldine iodomethylate in alkaline medium was described [1] Somewhat later [2], a dark-colored product [Formula (I) in Table], with an absorption maximum in alcoholic solution of 620mμ, was isolated by autooxidation reaction of hydroquinone in an aqueous solution of borate buffer in the presence of the quaternary salt of 2-methylbenzthiazole. Gates [3], by mixing benzene solutions of 1,4-naphthoquinone and a methylene base obtained from the quaternary quinaldine salt, isolated a compound [formula (XIII) in Table] which was not studied further.

Reaction of methylene heterocyclic nitrogen bases with quinones is an individual case of the condensation of a compound containing an active methyl or methylene group. It has been known for a long time [4] that acetoacetic ester, malonic ester, acetylacetone and similar compounds, when interacted with quinones, in the presence of alkalies, give dark-blue condensation products. The mechanism of this reaction consists first in addition of a molecule of the compound with an active methylene group to the quinone molecule, with formation of the derivative of the corresponding hydroquinone, which is then oxidized by a second quinone molecule to the substituted quinone. For the interaction of N-methyl-2-methylenebenzthiazoline and p-quinone, this reaction can be represented by the following scheme:



The hydroquinone corresponding to the quinone used is always found to be a side product of the condensation. Sometimes it is possible to isolate it, and sometimes it participates in the formation of dark, slightly soluble precipitates which are found to be compounds of the quinhydrone type.

It is not difficult to see that condensation products of methylene bases with quinones are quite close to dyes of the merocyanin class. The chromophore for the former and for the latter is of identical structure:



The former and the latter are representative of a number of intraionoidic dyes. As with the merocyanins, the condensation products between quinones and methylene bases are found to be polymethine dyes; however, compared to the typical polymethine dyes, they have received but little study.

The authors arranged to synthesize a series of compounds of this type, condensing methylene bases of various nitrogen heterocycles with various quinones. A synthetic method for these characteristic compounds, as well as their absorption curves in various solvents, and some of their conversions, was studied.

The synthetic method was quite simple. A benzene solution of the methylene bases resulted from the quaternary salt of the base taken. Sometimes chloroform was used as the solvent. The base solution was mixed with the quinone solution in the same solvent. The mixture was left at room temperature for 45 - 60 minutes. The resulting blue or blue-black product was filtered off and purified. Substances were always taken for reaction in the ratio of 1 mole of methylene base to 2 moles of quinone. If 1 mole of quinone is taken, the yield is approximately doubled. Upon prolonged standing, the intensely-colored solution became yellow-green, and a poorly-soluble residue, dark in color, was formed.

Low yields of pure products resulted upon interaction of methylene bases with p-benzoquinone, apparently related to formation of poorly-soluble compounds of the quinhydrone type. Solutions of methylene bases obtained from quaternary salts of 2-methylthiazole, 2-methyloxazole, α-picoline and 2,3,3-trimethylindolenine, when reacted with quinones, became intensely blue, without formation of precipitate, and coloration disappeared, especially in light. Anthraquinone and phenanthraquinone, with methylene bases of heterocyclic nitrogen under the conditions indicated, did not produce any colored products.

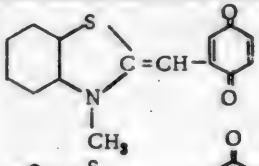
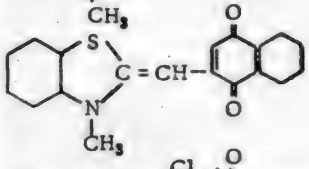
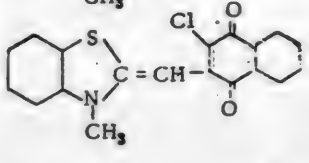
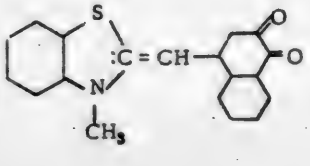
Formulas are given in the Table for compounds obtained by the authors, as well as their absorption maxima in alcohol, chloroform and alcohol containing added hydrochloric acid.

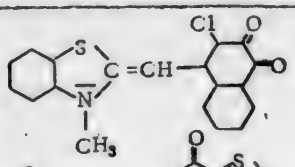
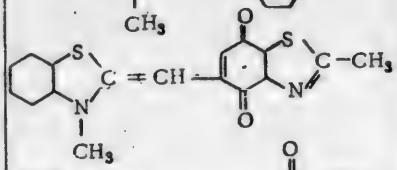
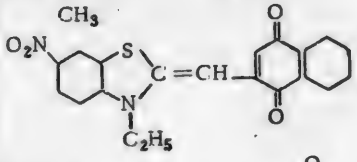
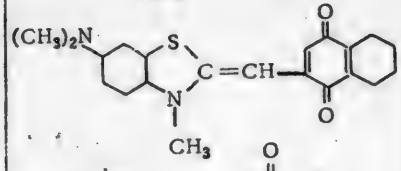
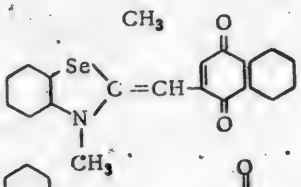
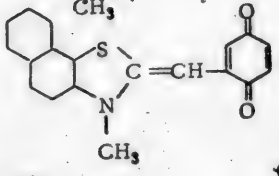
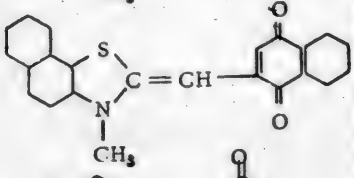
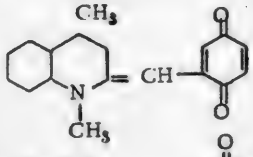
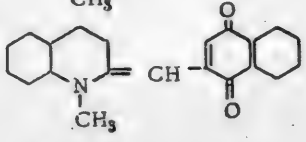
Absorption curves in alcohol and chloroform for the preparations given in the Table were broad, without sharp maxima. All preparations were deeply colored. Absorption maxima, as a rule, were about 600 mμ and higher. Deep coloration is a result of the quinoid ring present in the molecule. The corresponding merocyanins are less deeply colored.

Insofar as the condensation products of methylene bases with quinones are similar in structure to that of merocyanin it might be assumed that the rule established for relating color to structure for the merocyanins would also be accurate for the other compounds in question. Examination of the data in the Table confirms completely this assumption.

The properties of merocyanins as intraionoidic dyes has received considerable study. Their relation to various solvents has been studied, as well as the effects of various polar substituents upon the color of merocyanins. A theory generalizing and clarifying the mechanism has been developed [5].

As with the merocyanins the preparations given in the Table exhibit solvatochromy, i.e., they change color in neutral solvents in relation to the solvent used. As with the merocyanins, in these preparations the absorption maximum is displaced toward the short wave lengths upon transition from a solvent of higher dielectric constant (alcohol) to a solvent of lower dielectric constant (chloroform or benzene).

Number of compound	Formula for compound	Absorption maxima (in mμ)		
		In alcohol	in chloroform	In alcohol + hydrochloric acid
(I)		Insoluble	580	550
(II)		610	615	570
(III)		670	640	–
(IV)		640	620	430

Number of compounds	Formula for compound	Absorption maxima (in mμ)		
		In alcohol	In chloroform	In alcohol + HCl
(V)		650	645	420
(VI)		Insoluble	680	–
(VII)		Insoluble	560	–
(VIII)		680	660	620
(IX)		610	600	580
(X)		Insoluble	620	–
(XI)		640	630	580
(XII)		Insoluble	600	–
(XIII)		670	640	500

The rules established with merocyanins relative to the effect of polar substituents upon color, are also accurately reproducible for the condensation products between methylene bases and quinones.

Introduction of a negative group into the benzene ring of the nitrogen heterocycle displaces the absorption maximum to the short wave lengths [transition from preparation (II) to preparation (VII)]. Introduction of a negative substituent into the quinone ring, on the other hand, gives displacement of the absorption maximum toward the long wave lengths (transition from (II) to (III) and from (IV) to (V)). The replacement of hydrogen atoms in the heterocyclic radical by a positive group invokes a strong intensification of the color [transition from (II) to (VIII)]. The

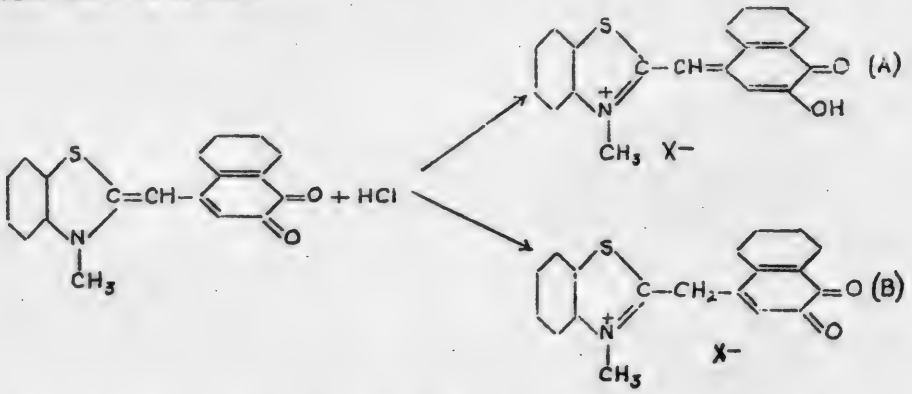
replacement of a less basic heterocyclic radical by a more basic gives the same effect [transition from (I) to (XII) and from (II) to (XIII)].

All of these facts can be readily summarized by the following statement: the more polar their molecules (the more positive the nitrogen heterocyclic radical and the more negative the quinone radical) the deeper the color of condensation products between methylene bases and quinones.

The condensation products of methylene bases with quinones give, under the action of mineral acids, salts, which can be observed by a sharp color change in their alcoholic solutions upon addition of a drop of hydrochloric acid. In converting from base to salt, the absorption maximum for an alcoholic solution is displaced (without fail) toward the short wave lengths.

Absorption maxima for hydrochloride salts are given in the last column of the Table.

The authors isolated and analyzed in their individual states the three corresponding perchlorates obtained by addition of sodium perchlorate solution to hydrochloride salt solutions of preparations (II), (III) and (XIII). Analysis indicated that one molecule of acid was combined with one molecule of base. The question of structure for these salts was solved on grounds of spectroscopic observations. In formation of a salt from the condensation product between methylene base and quinone, the proton of the acid can add either to the methine group, or to one of the oxygen atoms, for example:



It is not difficult to observe that salts of the (B) type, where conjugation of the two rings is ruptured, should be weakly colored, and that their absorption curve should be similar to the absorption curve for corresponding quinones. On the other hand, coloration for salts of type (A) should be deeper and more intense.

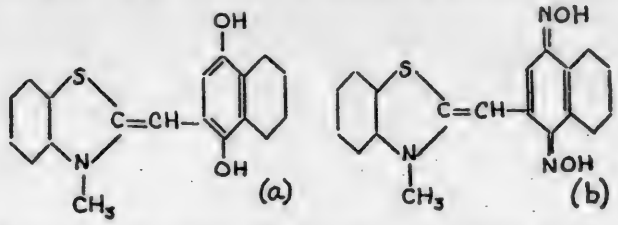
It can be seen from the absorption maxima of the salts given in Table that salts of preparations I, II, VIII, IX, XI and XIII have structures corresponding to type (A). With regards to salts of preparations (IV) and (V), then, judging from the yellow color of their solutions, and by their absorption maxima, which are close to the absorption maxima for the corresonding quinones, it might be assumed that their structure corresponds to type (B). By measuring the absorption intensity for these two salts, it is possible to solve the question of structure identity.

The absorption curves for alcoholic solutions of one and the same molecular concentration of preparation (IV), and its corresponding quinone (1,2-naphthoquinone) were measured, and one drop of hydrochloric acid was added to a solution of preparation (IV). It was found that the absorption intensity for the salt was 4.4 times greater than the intensity for quinone absorption, although the absorption maxima differed only by 5 mμ. Similar measurements were carried out with salt solutions of preparation (V) and of 3-chloro-1,2-naphthoquinone, where it was found that in this case absorption intensities are almost identical, the absorption curves were similar, and the maxima differ by only 7 mμ. It follows from these data that preparation (IV) gives with hydrochloric acid a salt corresponding to type (A), and preparation (V) corresponding to type (B). Such difference in relationship between preparations (IV) and (V) with regard to acid is apparently explicable by the fact that preparation (V), under the influence of a chlorine atom, possesses depressed basic properties for the quinone ring.

The condensation products of methylene bases with quinones are readily reduced with decolorization, converting to the corresponding hydroquinone derivative. Reduction can be effected with sodium bisulfite in alkaline solution. The resulting colorless or light-yellow solution possessed the properties of Cuba wood. Tissue paper moistened with the solution became colored rapidly in the air, acquiring the color of the dye used in the reduction. Reduction can also be carried out with tin and hydrochloric acid.

The authors obtained the dihydroxylderivative (a) from product (II) upon its reduction by the first and second methods.

Its structure was proved by its conversion to diacetyl and dimethoxy derivatives.



From the same preparation (II) there was obtained, by heating it with hydroxylamine hydrochloride, a yellow crystalline dioxime (b).

EXPERIMENTAL

3-Chloro-1,2-naphthoquinone [6] was obtained by chlorination of 1,2-naphthoquinone in glacial acetic acid. Long red needles, m.p. 173°.

2,3-Dichloro-1,4-naphthoquinone [7] was prepared from α-naphtholsulfonic acid by treating it with Berthollet's salt and hydrochloric acid. Yellow needles with m.p. 193°.

2-Methyl-4,7-benzthiazolquinone. Synthesized according to Fried and Reitz [8]. Fine yellow needles, m.p. 159°.

Quaternary salts of the heterocyclic bases, containing an active methyl group in the α-position, were obtained from the corresponding bases by reacting with alkyl halides or dialkyl sulfates.

2-(3'-Methylbenzthiazolinylidene-2'-methyl)-1,4-benzoquinone (I). 0.27 g of potash in 2 ml of water and 10 ml of benzene were added to a solution of 0.27 g of methylmethosulfate 2-methylbenzthiazole in 2 ml of water. The mixture was shaken in a separatory funnel. After standing, the water layer was separated, and to the benzene solution of methylene bases there was added 0.21 g of 1,4-benzo quinone in 5 ml of benzene. The mixture was stirred and left for one hour. The colored product which precipitated was washed with water, boiling alcohol and then with ether. After crystallization from chloroform or benzene, violet crystals with metallic luster resulted, m.p. 237° (in this case, and others to follow, uncorrected melting points are given). Yield was 0.03 g (14%). The product was poorly soluble in alcohol and ether, better in chloroform and benzene, and insoluble in water.

Found %: N 5.13, 5.08. $C_{15}H_{11}O_2NS$. Calculated %: N 5.20.

2-(3'-Methylbenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone (II) was synthesized from 1 g of methylmethosulfate of 2-methylbenzthiazole, 1.35 g of potash and 1.15 g of 1,4-naphthoquinone, as in the preceding preparation. The product which precipitated out was washed with boiling alcohol and recrystallized from benzene. Long violet needles with copper luster, m.p. 247°, with decomposition. Yield was 1.02 g (88.3%).

Found %: N 4.19, 4.24. $C_{19}H_{13}O_2NS$. Calculated %: N 4.39.

To obtain the perchlorate, 0.2 g of resulting product was dissolved in benzene, and 3 drops of concentrated hydrochloric acid plus 3 ml of water added to the solution. After vigorous stirring, the water layer was separated, filtered, and an aqueous solution of sodium perchlorate added to it. The resulting red, amorphous precipitate was filtered off, dried and crystallized from absolute alcohol, m.p. 230°. Yield was 0.17 g (65%). The product hydrolyzed very readily with water and pure alcohol.

Found %: N 3.50, 3.52. $C_{19}H_{13}O_2NS \cdot HClO_4$. Calculated %: N 3.33

In order to obtain the 2-(3'-methylbenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone dioxime, a mixture of 0.2 g of this preparation and 0.2 g of hydroxylamine hydrochloride were heated on a water bath for 2 hours with 1.5 ml of pyridine and 1.5 ml of absolute alcohol. The blue solution became yellow. It was evaporated to dryness, and 3 ml of water added to the residue. The part which did not dissolve in water was filtered and recrystallized from dilute alcohol. Orange-yellow, finely crystalline powder, m.p. 73°. Yield was 0.07 g (33%).

Found %: N 11.92, 11.95. $C_{19}H_{15}O_2N_3S$. Calculated %: N 12.03.

2-(3'-Methylbenzthiazolinylidene-2'-methyl)-1,4-naphthohydroquinone. a) 0.4 g of 2-(3'-methylbenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone in 10 ml of alcohol was heated with 4 ml of concentrated hydrochloric acid and 0.4 g of stannous chloride, to the formation of a transparent light-yellow solution. After cooling, a crystalline precipitate separated, which was filtered, washed with water, dried, and recrystallized from dilute alcohol. Large colorless crystals, with m.p. 167°, with decomposition, resulted. Yield was 0.32 g (80%). The alkaline solution of the preparation oxidized readily, converting to a blue product.

b) 0.2 g of 2-(3'-methylbenzthiazolinylidine-2-methyl)-1,4-naphthoquinone was mixed with 0.4 g of caustic soda in 20 ml of water, and treated in a stream of illuminating gas with 0.4 g of sodium bisulfite and gentle heating and stirring. After 30 minutes, a yellow solution was formed which, after cooling, was neutralized with dilute hydrochloric acid by use of Congo red indicator. The resulting amorphous precipitate was filtered off, dried and crystallized from dilute alcohol. Colorless, crystalline powder, m.p. 167°, with decomposition. Yield was 0.13 g (65%).

To obtain the diacetyl derivative, 0.2 g of this hydroquinone was heated with 1 ml of acetic anhydride on a boiling water bath for 2 hours. After cooling, 3 ml of water was added to the mixture. The resulting product was filtered off, washed with water, and dried. After crystallization from 50% alcohol, colorless crystals with m.p. 144°. Yield was 0.2 g (83%).

Found %: N 3.54, 3.58. $C_{23}H_{19}O_4NS$. Calculated %: N 3.47.

Dimethyl Ester of 2-(3'-methylbenzthiazolinylidene-2'-methyl)-1,4-naphthohydroquinone. An alkaline solution of 2-(3'-methylbenzthiazolinylidene-2'-methyl)-1,4-naphthohydroquinone in an atmosphere of illuminating gas was treated with dimethyl sulfate excess. The resulting voluminous precipitate was filtered off and recrystallized from alcohol. A yellow crystalline product, m.p. 54°. Yield was 0.16 g (76%).

Found %: N 3.86, 3.87. $C_{21}H_{19}O_2NS$. Calculated %: N 4.01.

2-(3'-Methylbenzthiazolinylidene-2'-methyl)-3-chloro-1,4-naphthoquinone (III). 0.27 g of 2-methylbenzthiazol methylmethosulfate in 10 ml of water was shaken in a separatory funnel with 0.22 g of 2,3-dichloro-1,4 naphthoquinone [7] in 10 ml of chloroform and 0.27 g of potash in 5 ml of water. The aqueous layer was separated, and from the blue chloroform solution a precipitate separated after 1 hour which was filtered and recrystallized from chloroform. Blue crystals, m.p. 194°. Yield was 0.14 g. (41%).

Found %: N 4.11, 4.13; Cl 10.03, 10.02. $C_{19}H_{12}O_2NSCl$. Calculated %: N 3.96, Cl 10.04.

The perchlorate was obtained from an alcoholic solution of the hydrochloride salt by reacting the solution with sodium perchlorate. 0.24 g (68%) of light-yellow crystalline powder with m.p. 203-204° was isolated from 0.3 g of the preparation after recrystallization from absolute alcohol.

Found %: N 2.90, 2.95; Cl 15.30, 15.27. $C_{19}H_{12}O_2NSCl \cdot HClO_4$. Calculated %: N 3.08; Cl 15.63.

4-(3'-Methylbenzthiazolinylidene-2'-methyl)-1,2-naphthoquinone (IV) was obtained from 0.27 g of 2-methylbenzthiazole methylmetho sulfate, 0.27 g of potash and 0.31 g of 1,2-naphthoquinone as before. Fine blue crystals with m.p. 223°. Yield was 0.1 g. (32%).

Found %: N 4.10, 4.12. $C_{19}H_{13}O_2NS$. Calculated %: N 4.39.

4-(3'-Methylbenzthiazolinylidene-2'-methyl)-3-chloro-1,2-naphthoquinone (V) was obtained from 0.27 g of 2-methylbenzthiazole methyl methosulfate, 0.27 g of potash and 0.19 g of 3-chloro-1,2-naphthoquinone as with the preceding. After boiling with alcohol, the product was recrystallized from chloroform. Fine crystals, m.p. 151°. Yield was 0.08 g. (23%).

Found %: N 3.77, 3.75; Cl 9.87, 9.80. $C_{19}H_{12}NSCl$. Calculated %: N 3.96; Cl 10.04.

5-(3'-Methylbenzthiazolinylidene-2'-methyl)-2-methyl-4,7-benzthiazolquinone (VI). Obtained from 0.26 g of 2-methylbenzthiazole methyl methosulfate, 0.47 g of potash and 0.3 g of 2-methyl-4,7-benzthiazolquinone, as in the preceding. The condensation product was recrystallized from benzene. Blue needles with m.p. 234-235°. Yield was 0.16 g (50%).

Found %: N 8.04, 8.10. $C_{17}H_{12}O_2N_2S_2$. Calculated %: N 8.23.

2-(3'-Ethyl-6'-nitrobenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone (VII) was synthesized from 0.35 g of 2-methyl-6-nitrobenzthiazole iodoethylate, 0.31 g of 1,4-naphthoquinone and 0.27 g of potash. Red crystals with copper luster, m.p. 309°. Yield was 0.08 g (22%).

Found %: N 7.19, 7.22. $C_{20}H_{14}O_4N_2S$. Calculated %: N 7.40.

2-(3'-Methyl-6'-dimethylaminobenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone (VIII) was synthesized from 0.33 g of iodomethylate of 2-methyl-6-dimethylaminobenzthiazole, 0.31 g of 1,4-naphthoquinone and 0.27 g of potash as with preceding. After boiling with alcohol, and crystallizing from benzene, green platelets with m.p. 216° resulted. Yield was 0.09 g (26%).

Found %: N 7.55, 7.50. $C_{21}H_{18}O_2N_2S$. Calculated %: N 7.73.

2-(3'-Methylbenzselenazolinylidene-2'-methyl)-1,4-naphthoquinone (IX) was obtained from 0.32 g of 2-methylbenzselenazole methylmethosulfate, 0.27 g of potash and 0.31 g of 1,4-naphthoquinone. Fine blue crystals with m.p. 172°, with decomposition. Yield was 0.13 g (36%).

Found %: N 3.65, 3.68. $C_{19}N_{13}O_2NSe$. Calculated %: N 3.82.

2-(3'-Methyl-6',7'-benzobenzthiazolinylidene-2'-methyl)-1,4-benzoquinone (X). Obtained from 0.64 g of 2-methyl-6,7-benzobenzthiazole methyl metho sulfate, 0.54 g of potash and 0.42 g of 1,4-benzoquinone. Violet, fine crystalline powder, m.p. 209°, with decomposition. Yield was 0.2 g. (32%).

Found %: N 4.48, 4.51. $C_{19}H_{13}O_2NS$. Calculated %: N 4.38.

2-(3'-Methyl-6',7'-benzobenzthiazolinylidene-2'-methyl)-1,4-naphthoquinone (XI), was obtained from 0.32 g of 2-methyl-6,7-benzobenzthiazole methyl methosulfate, 0.27 g of potash and 0.31 g of 1,4-naphthoquinone. Fine blue crystals with copper luster, m.p. 246°. Yield was 0.16 g (44%).

Found %: N 3.95, 4.00. $C_{23}H_{15}O_2NS$. Calculated %: N 3.79.

2-(1'-Methylquinolylidene-2'-methyl)-1,4-benzoquinone (XII) was obtained from 0.54 g of quinaldine methyl methosulfate, 0.24 g of sodium hydroxide and 0.42 g of 1,4-benzoquinone. Fine blue crystals, m.p. 169°, with decomposition. Yield was 0.09 g (17%).

Found %: N 5.14, 5.16. $C_{17}H_{13}O_2N$. Calculated %: N 5.32

2-(1'-Methylquinolylidene-2'-methyl)-1,4-naphthoquinone (XIII) was obtained from 1.08 g of quinaldine methylmethosulfate, 0.48 g of sodium hydroxide and 1.21 g of 1,4-naphthoquinone. Violet needles with golden luster, m.p. 178°. Yield was 0.31 g (26%).

Found %: N 4.60, 4.53. $C_{21}H_{15}O_2N$. Calculated %: N 4.47.

The perchlorate was obtained by addition of sodium perchlorate to a solution of the base in hydrochloric acid. After recrystallization from absolute alcohol, there resulted fine red crystals, m.p. 207°, with decomposition. Yield was 0.13 g (50%).

Found %: N 3.19, 3.17; Cl 8.54, 8.60. $C_{21}H_{15}O_2N \cdot HClO_4$. Calculated %: N 3.38; Cl 8.82.

SUMMARY

13 condensation products have been obtained by reacting methylene heterocyclic nitrogen bases with 1,4-benzoquinone, 1,2- and 1,4-naphthoquinones, and their chlorine substitution products, as well as with 2-methyl-4,?-benzthiazolquinone, representing intraionoidic dyes of the merocyanin type. The absorption maxima for these dyes in neutral and acid solutions have been determined.

Perchlorates and other derivatives have been obtained from some of the condensation products of methylene bases with quinone.

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PHENYLAMIDATION OF DIBASIC CARBOXYLIC ACIDS WITH DIPHENYLSULFAMIDE

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It was found recently that upon reacting a sulfamide with dibasic carboxylic acids, there is formed, depending upon the structure of the acid, either the diamide of the dicarboxylic acid, or the imide [1]. In this work the reaction of diphenylsulfamide with dicarboxylic acids was studied. It was found that the sulfamide reaction and the diphenylsulfamide reaction with dicarboxylic acids was not the same. Thus, reaction of sulfamide with oxalic acid resulted in evolution of carbon dioxide, but neither formamide nor formamidine (compare [2]), nor oxamic acid, nor oxamide separated [1]. Upon reacting diphenylsulfamide with oxalic acid, carbon dioxide was evolved, but along with rupture of oxalic acid there also proceeded phenylamidation, and the oxalic acid dianilide was formed, although in small yields (25%). Reacting sulfamide with dicarboxylic acids readily giving internal anhydrides (succinic, glutaric, phthalic) gave only cyclic imides (along with succinamic acid in the case of succinic acid) [1]. Diphenylsulfamide reacted with phthalic acid and with its anhydride to give the phenylamide, but with succinic and glutaric acids, it gave dianilides instead of phenylamides. It is of interest that malonic acid gave only acetamide with sulfamide – it was not possible to isolate malonamide. With diphenylsulfamide, malonic acid gave the dianilide of malonic acid only – acetanilide failing to separate. Thus, sulfamide caused rupture of malonic acid, and diphenylsulfamide reacted with the former without splitting off carbon dioxide. Sulfamide and diphenylsulfamide reacted analogously with diethylmalonic acid – carbon dioxide being split off in both cases, with formation of diethylacetic acid amide and anilide. Isophthalic acid reacted normally with diphenylsulfamide.

Thus, in the amidation of dibasic acids with sulfamides, the formation of cyclic imides (succinic, glutaric and phthalic acids) proceeded more rapidly, and carbon dioxide was split off more rapidly (oxalic and malonic acids). Dianilides were more readily formed upon phenylamidation (oxalic, succinic and glutaric acids) and carbon dioxide split out with greater difficulty. Formation of cyclic phenylimides upon phenylamidation took place only for acids which form anhydrides with exceptional ease (phthalic, but not succinic or glutaric).

Phenylamidation of dibasic carboxylic acids proceeds under mild conditions and in good yields (with the exception of oxalic acid), and can be readily carried out with very small amounts of substance, and therefore can be recommended for identification of dicarboxylic acids, taking into particular account the fact that dianilides of an impressive majority of dicarboxylic acids are poorly soluble, high melting and crystallize readily.

EXPERIMENTAL

Phenylamidation of Dibasic Acids with Diphenylsulfamide. A mixture of 0.005 mole of dicarboxylic acid and 0.01 mole of diphenylsulfamide (2.48 g) was heated with 5.0 ml of pyridine for 4 hours (in some cases 6 hours) on an oil bath at 115-120° (in some cases 100 or 80°). Pyridine was distilled off from a water bath in vacuo, the residue treated with 5.0 ml of 1N sodium hydroxide solution, the residue sucked dry by filtration and washed with water. For purification, the reaction product was recrystallized from a suitable solvent.

Thus there resulted:

1) From oxalic acid – the dianilide of oxalic acid, m.p. 245-246° after recrystallization from benzene (uncorrected); the yield was 14% of theory (reaction at 115-120° for 4 hours), 19.3% (at 80°, 10 hours), 25% (at 70°, 6-10 hours).

2) From malonic acid – the dianilide of malonic acid, m.p. 222-223° after recrystallization from alcohol (uncorrected); yield was from 73.2 to 75.5% of theory (reaction at 115-120°, 100 and 80°, 4 and 10 hours).

3) From diethylmalonic acid – the anilide of diethylacetic acid, m.p. 122-124° after recrystallization from carbon tetrachloride (unconected); yield 95.0% of theory.

4) From succinic acid – the dianilide of succinic acid, m.p. 226-228° uncorrected after recrystallization from alcohol; yield was 67.1 and 82.7% of theory (reaction at 115-120° and at 100°, 4 hours).

5) From glutaric acid – the dianilide of glutaric acid, m.p. 221-222° after recrystallization from alcohol (uncorrected); yield 86.0% of theory.

6) From adipic acid – adipic acid dianilide, m.p. 234-236° after recrystallization from alcohol (uncorrected); yield was 84.4% of theory.

7) From phthalic acid or from phthalic anhydride – phenylphthalimide, m.p. 202-203° (uncorrected) after recrystallization from alcohol; yield was 96.8% of theory.

8) From isophthalic acid – the dianilide of isophthalic acid, m.p. 275-276° from acetic acid after recrystallization; yield was 96.8% of theory.

All of the substances were identified according to the melting point for a mixed sample with known pure preparations.

According to the literature data, isophthalic acid dianilide melts at 250° [3]. For comparison, the dianilide of isophthalic acid was prepared from the dichloroanhydride of isophthalic acid and aniline excess in benzene solution. The preparation synthesized according to this method, like a sample mixed with the substance which was obtained by direct phenylamidation, melted at 275-276° (uncorrected). Thus the literature data [3] are inaccurate; in actuality, the dianilide of isophthalic acid melts at 275-276° (uncorrected).

Amidation of Diethylmalonic Acid with Sulfamide. Amidation of diethylmalonic acid was carried out in order to compare the reaction of sulfamide and of diphenylsulfamide with this acid. A mixture of 0.01 mole of diethylmalonic acid (1.61 g), 0.02 mole of sulfamide (1.92 g) and 5.0 ml of dry pyridine was heated on a boiling water bath for 3 hours. Pyridine was distilled off in vacuo, and to the residue was added 10 ml of a 2N solution of soda, and the water evaporated in vacuo at 40°. Diethylacetic acid amide was extracted from the dry residue by ether. Yield was 0.95 g, i.e., 82.5% of theory. After recrystallization from alcohol, m.p. was 105-106° (uncorrected), which corresponded to the literature data [4].

SUMMARY

1. The reaction of diphenylsulfamide with dicarboxylic acids has been studied.

2. It has been demonstrated that dianilides result in good yields from phenylamidation of oxalic, malonic, succinic, glutaric, adipic and isophthalic acids, using diphenylsulfamide.

3. Phthalic acid and its anhydride form phenylamide upon phenylamidation.

4. Diethylmalonic acid upon phenylamidation gives the anilide of diethylacetic acid.

5. Direct phenylamidation of a dicarboxylic acid can be used for purposes of identification with considerable success.

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•• See Consultants Bureau Translation, p. 1653.

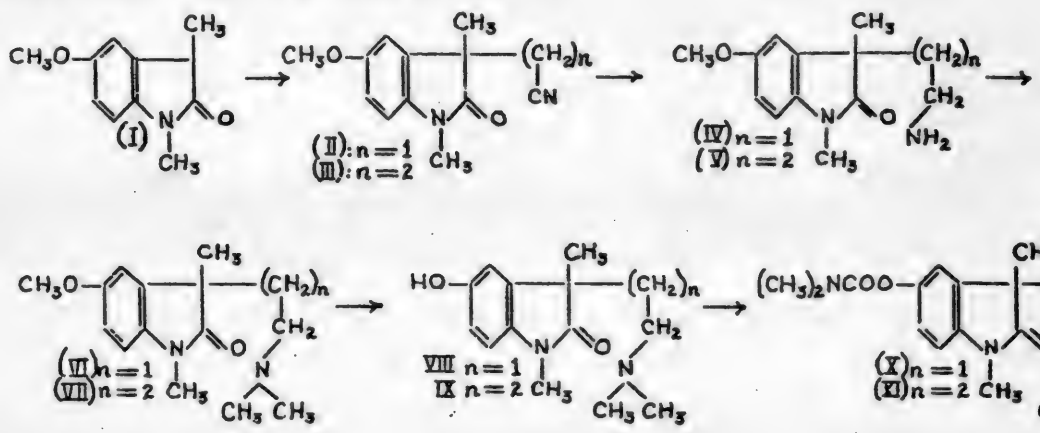
SYNTHETIC INVESTIGATION IN THE INDOLE DERIVATIVE SERIES

III. SYNTHESIS OF 1,3-DIMETHYL-3-β-DIMETHYLAMINOETHYL-5-HYDROXYINDOLIN-2-ONE (DEHYDROESEROLINMETHINE) AND 1,3-DIMETHYL-3-γ-DIMETHYLAMINOPROPYL-5-HYDROXYINDOLIN-2-ONE (DEHYDROHOMOESEROLINMETHINE) URETHANES

M. N. Kolosov and N. A. Preobrazhensky

The simplest eserine-like substances known up to the present time could be divided perhaps into two large groups, depending upon the nature of the base of which they are derivatives. The first group is composed of weakly basic eserine analogs, in which the amino group is tied up with the aromatic ring – carbamine esters of substituted aniline, indolines, pyridines, quinolines, and so forth. To the second group could belong urethanes of phenols which possess an amino group in the side chain, and which are related to those stronger bases – the myotine-type substances. For all compounds of the first group there is the characteristic shortcoming that their salts, with the exception of some quaternary salts, hydrolyze readily in aqueous solution, due to which fact rapid inactivation of the preparations occurs. Compounds of the second group are far-removed from eserine in their structure, and are not in the full sense of this word, analogs of the alkaloid.

With consideration for the above state of affairs, the authors decided to investigate urethanes of the 5-hydroxyindoline series, which possess an amino group in the side chain, and which at the same time are found to be derivatives of p-aminophenol which approximate eserine structurally. As such, the first group selected was the dimethylurethanes of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one (dehydroeserolinmethine) (X) and 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one (dehydrohomoeserolinmethine) (XI), synthesis of which is described in the present article.



1,3-Dimethyl-5-methoxyindolin-2-one (I) was condensed with chloroacetonitrile [1], the condensation product (II) hydrogenated over skeletal nickel catalyst in the presence of ammonia, and the primary amine (IV) was converted into the tertiary base (VI) upon methylation with formaldehyde and formic acid; the same 1,3-dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one (dehydroeserometolmethine) (VI) was obtained upon treating the sodium derivative of hydroxyindole (I) with chloroethyldimethylamine. After hydrolysis of the ester, rearrangement of compound (VI) by hydrobromic acid to 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one (dehydroeserolinmethine)(VIII) took place, the sodium phenolate of which, with dimethylcarbamic acid chloroanhydride, gave the dimethylurethane of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one (X). Synthesis of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one dimethylurethane (XI) was carried out in similar fashion, whereupon the nitrile (III) was obtained by condensation of hydroxyindole (I) with acrylonitrile in the presence of catalytic amounts of trimethylbenzylammonia ("triton B") base.

A study of the myotic effect of eserine analogs described in the present work as carried out on rabbits gave the following threshold concentration values for the substance in question•: hydrochloride (X) – 1: 5000; iodomethylate (X) – 1: 5000; hydrochloride (XI) – 1: 500.

EXPERIMENTAL

1) 1,3-Dimethyl-3-cyanomethyl-5-methoxyindolin-2-one (II). 15.8 g (2.92 gram atoms) of sodium in 500 ml of absolute alcohol was added over a period of 4 hours to a solution consisting of 45.0 g (1.00 mole) of 1,3-dimethyl-5-methoxyindolin-2-one in 200 ml of absolute alcohol and 50.0 g (2.81 moles) of chloroacetonitrile [2] stirred at 60°. After standing for 1 hour at the same temperature, the alcohol was distilled off in vacuo and the residue was dissolved, with shaking, in 120 ml of water and 200 ml of ether. The aqueous layer was extracted with ether, the ether solutions combined, dried with sodium sulfate and evaporated, and the residue was distilled. 50.3 g of viscous yellowish oil with b.p. 203-205° at 7 mm resulted. It was crystallized by grinding with a small amount of ether and then recrystallized from the same solvent. The yield of 1,3-dimethyl-3-cyanomethyl-5-methoxyindolin-2-one was 44.1 g (81%), m.p. 74.5-75.0°.

3.110 mg substance: 7.760 mg CO_2; 1.635 mg H_2O. 3.770 mg substance: 0.422 ml N_2 (24°, 735 mm). Found %: C 68.04; H 5.90; N 12.44. $C_{13}H_{16}O_2N_2$. Calculated %: C 67.80; H 6.13; N 12.17.

2) 1,3-Dimethyl-3-β-aminoethyl-5-methoxyindolin-2-one (IV). 20.0 g of 1,3-dimethyl-3-cyanomethyl-5-methoxyindolin-2-one, a solution of saturated ammonia in 70 ml of absolute methanol at 0° and 2 g of a skeletal nickel catalyst were placed in a rocking autoclave of 200 ml capacity. The autoclave was filled with hydrogen to 120 atmospheres and was heated with shaking for 4 hours at 105-110°. After cooling, the solution was separated from catalyst by filtration, evaporated, and the residue distilled. 17.8 g (88%) of 1,3-dimethyl-3-β-aminoethyl-5-methoxyindolin-2-one resulted, b.p. 201-203° and 9 mm (compare [3]).

3.315 mg substance: 8.100 mg CO_2; 2.195 mg H_2O. 4.675 mg substance: 0.500 ml N_2 (25°, 734 mm). Found %: C 66.63; H 7.41; N 11.83. $C_{13}H_{18}O_2N_2$. Calculated %: C 66.67; H 7.45; N 11.96.

Picrate was obtained from alcoholic solution and recrystallized from alcohol – yellow crystals with m.p. 161-162° (compare [3]).

Hydrogen iodide salt was obtained from an alcoholic solution of the base with hydrogen iodide and precipitation with ether. After recrystallizing from alcohol, it was found to be in the form of colorless crystals with m.p. 189-190°.

3.070 mg substance: 4.845 mg CO_2; 1.440 mg H_2O. 4.725 mg substance: 0.343 ml N_2 (20°, 725 mm). Found %: C 43.04; H 5.25; N 8.07. $C_{13}H_{19}O_2N_2I$. Calculated %: C 43.09; H 5.29; N 7.73.

3) 1,3-Dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one (dehydroesermetolmethine (VI).

A. From 1,3-Dimethyl-3-β-aminoethyl-5-methoxyindolin-2-one. 17.0 g of 1,3-dimethyl-3-β-aminoethyl-5-methoxyindolin-2-one was dissolved in 18 ml of 90% formic acid, 16 ml of 40% aqueous formaldehyde solution added, and the reaction mixture heated on a metal bath at 110-115° for 6 hours. The solution formed was evaporated in vacuo on a water bath, the residue made alkaline with 20% potassium hydroxide solution to phenolphthalein alkaline color, and the oil which separated was extracted with ether. The extract was washed with water, dried with sodium sulfate, the ether distilled off, and the residue distilled in vacuo. 13.4 g (70%) of 1,3-dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one resulted with b.p. 210-215° at 20 mm.

B. From 1,3-Dimethyl-5-methoxyindolin-2-one. 20.0 g (1.00 mole) of 1,3-dimethyl-5-methoxyindolin-2-one and 1 ml of absolute alcohol were added to a suspension of 2.5 g (1.04 gram atoms) of pulverized sodium in 150 ml of absolute toluene and the mixture heated, with stirring, to boiling. After holding for 1 hour, 17.0 g (1.51 moles) of freshly-distilled chloroethyldimethylamine (b.p. 108-109°) was added over a period of 10 minutes, and stirring was continued at the same temperature for another hour. After cooling, the base was extracted with 10% hydrochloric acid (3 times with 30 ml portions), the toluene solution washed with a small volume of water, and the combined acid extract made alkaline with a 40% solution of sodium hydroxide. The oil which separated was extracted with ether, the extract dried with sodium sulfate, the ether distilled off, and the residue distilled.

• Investigation of the compounds synthesized in the present work with respect to their physiological activity was carried out in the S. Ordzhonikidze All-Union Chemico-Pharmaceutical Research Institute by a senior scientific co-worker, I. M. Sharapov, directed by Prof. M. D. Mashkovsky, to whom the authors wish to express sincere appreciation.

22.8 g (83%) of 1,3-dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one, with b.p. 140-143° at 2 mm was obtained.

Hydrochloride was obtained by saturation with dry hydrogen chloride of the base dissolved in an equal volume of alcohol. After recrystallization from ethanol, it was in the form of colorless crystals with m.p. 199.0-199.5°.

4.130 mg substance: 0.334 ml N_2 (17°, 750 mm). 3.885 mg substance: 0.314 ml N_2 (23°, 740 mm).
Found %: N 9.40, 9.08. $C_{15}H_{23}O_2N_2Cl$. Calculated %: N 9.37.

Methyl iodide salt resulted from the addition of methyl iodide in excess to a solution of the base in dry acetone. After 10-15 minutes, dry ether was added to the point of light turbidity; on standing, colorless crystals precipitated. After recrystallization from absolute alcohol, the methyl iodide addition product had an m.p. of 156.0-156.5° (compare [4]).

Picrate was obtained from alcoholic solution and recrystallized from alcohol. It was in the form of bright-yellow crystals with m.p. 171.0-171.5°.

Methylpicrate was formed by heating an alcoholic solution of methyl iodide with picric acid excess. After recrystallization from a large volume of alcohol, it was in the form of lustrous yellow crystals with m.p. 194-195° (compare [4]).

4) 1,3-Dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one (dehydroeserolinmethine) (VIII). 5.0 g of 1,3-dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one hydrochloride was heated with 25 ml of 50% hydrobromic acid on a metal bath at 135-140° for 2 hours. The hydrobromic acid was then distilled in vacuo on a water bath, the residue dissolved in methanol, and precipitated with ether. The mother liquors were evaporated and treated in a similar manner. After recrystallization from absolute alcohol, there resulted 5.16 g (94%) of 1,3-dimethyl-3-β-dimethylaminoethyl-5- hydroxyindolin-2-one hydrobromide, colorless crystals with m.p. 186.0-186.5°.

2.034 mg substance: 0.294 ml N_2 (21°, 748 mm). 3.820 mg substance: 0.274 ml N_2 (21°, 748 mm).
Found %: N 8.33, 8.20. $C_{14}H_{21}O_2N_2Br$. Calculated %: N 8.51.

To separate the base, an alcoholic solution of the hydrobromide was mixed with an alcoholic solution of the calculated amount of potassium hydroxide, and then with a 10-fold volume of dry ether. The resulting crystals were filtered off. The filtrate was evaporated and the residue recrystallized from alcohol. 1,3-Dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one was in the form of colorless crystals with m.p. 170.0-170.5°; readily soluble in aqueous solutions of acids and alkalies, as well as in alcohol and chloroform, and poorly soluble in water and ether. The substance was best extracted from aqueous solutions with butyl alcohol.

4.765 mg substance: 0.461 ml N_2 (21°, 751 mm). 4.440 mg substance: 0.441 ml N_2 (21°, 751 mm).
Found %: N 11.07, 11.36. $C_{14}H_{20}O_2N_2$. Calculated %: N 11.28.

Picrate was obtained from alcoholic solution. It crystallized from alcohol in the form of yellow needles with m.p. 177-178°.

The hydrochloride was obtained by the addition of an alcoholic solution of hydrogen chloride to an alcoholic solution of the base, and precipitated by ether. After recrystallization from alcohol, it was in the form of colorless crystals with m.p. 240.0-240.5°.

3.745 mg substance: 0.314 ml N_2 (21°, 751 mm). 3.008 mg substance: 0.255 ml N_2 (22°, 747 mm).
Found %: N 9.59, 9.64. $C_{15}H_{21}O_2N_2Cl$. Calculated %: N 9.84.

5) Dimethylcarbamic Ester of 1,3-Dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one (dimethylurethane of dehydroeserolinmethine) (X). 3.00 g (1.00 mole) of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one was dissolved, with heat, in 10 ml of absolute methyl alcohol, and was mixed with a solution of 1.00 g (2.03 moles) of sodium methylate in 10 ml of methanol. The mixture was evaporated to dryness in vacuo, with heat from a water bath. The solid residue was finely-ground and suspended in 25 ml of absolute benzene. 1.50 g (1.53 moles) of dimethylcarbamic acid chloroanhydride was added and the reaction mass left for 48 hours at room temperature, after which it was heated for 2 hours on a water bath to complete reaction. The hot solution was filtered off from the sodium chloride and bromide, the precipitate washed with absolute benzene, the filtrate evaporated in vacuo, and the residue after distilling off the benzene, was shaken with 50 ml of absolute ether; thereupon white curds of precipitate (0.7 g) separated, which darkened and melted in the air. After the addition of an alcoholic

solution of hydrogen chloride to the ether filtrate, there precipitated a viscous precipitate of urethane hydrochloride, which then gradually solidified. After several precipitations with ether from alcoholic solution, we obtained 2.65 g (82%) of the dimethylcarbamic ester of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one hydrochloride, colorless crystals resulted with m.p. 211-212°.

3.500 mg substance: 0.348 ml N_2 (19°, 753 mm). 3.895 mg substance: 0.402 ml N_2 (21°, 751 mm). Found %: N 11.52, 11.81. $C_{17}H_{26}O_3N_3Cl$. Calculated %: N 11.81.

Picrate resulted from alcoholic solutions of the hydrochloride and picric acid. It crystallized from alcohol in the form of yellow needles with m.p. 193.5-194.0°.

To obtain the methyl iodide of the urethane, the hydrochloride was treated with an alcoholic solution of sodium methylate, the reaction mass diluted with a 10-fold volume of absolute ether, and removed from the sodium chloride by filtration. The filtrate was evaporated, the technical base (m.p. 83-84°) dissolved in dry ether, to which had been added several drops of alcohol, and methyl iodide added. The resulting precipitate was filtered off with suction, precipitated several times with ether from alcohol, and recrystallized from absolute alcohol. 0.10 g of sodium methylate, 0.5 ml of CH_3I and 0.68 g of the hydrochloride yielded 0.72 g of the dimethylcarbamic ester methyl iodide of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one, with m.p. 201-202°.

4.650 mg substance: 0.360 ml N_2 (21°, 751 mm). 3.945 mg substance: 0.306 ml N_2 (21°, 751 mm). Found %: N 8.86, 8.87. $C_{18}H_{29}O_3N_3I$. Calculated %: N 9.11.

6) 1,3-Dimethyl-3-β-cyanoethyl-5-methoxyindolin-2-one (III). 20.4 g (1.02 moles) of acrylonitrile was added to 72.0 g (1.00 mole) of 1,3-dimethyl-5-methoxyindolin-2-one solution and 3.6 g of 40% aqueous trimethylbenzylammonia base solution in 215 ml of dry dioxane, stirred, cooled with ice, the addition rate being such that the temperature of the reaction mixture did not rise above 15°. Stirring was continued for another 4 hours at room temperature, after which the dioxane was distilled in vacuo and the residue purified by crystallization from a mixture of ether and methyl alcohol. There resulted 81 g (88%) of 1,3-dimethyl-3-cyanoethyl-5-methoxyindolin-2-one with m.p. 89-90° and a b.p. of 178-180° at 1 mm; in mixture with 1,3-dimethyl-5-methoxyindolin-2-one, it gave an m.p. of 61-63°.

3.155 mg substance: 7.980 mg CO_2; 1.815 mg H_2O. 2.975 mg substance: 7.550 mg CO_2; 1.675 mg H_2O. 3.140 mg substance: 0.328 ml N_2 (21°, 725 mm). 3.090 mg substance: 0.329 ml N_2 (21°, 725 mm). Found %: C 68.97, 69.10; H 6.43, 6.30; N 11.56, 11.51. $C_{14}H_{16}O_2N_2$. Calculated %: C 68.82; H 6.60; N 11.47.

7) 1,3-Dimethyl-3-γ-aminopropyl-5-methoxyindolin-2-one (V). 20.0 g of 1,3-dimethyl-3-β-cyanoethyl-5-methoxyindolin-2-one was hydrogenated in the presence of 2 g of skeletal nickel catalyst under the conditions described for synthesis of 1,3-dimethyl-3-β-aminoethyl-5-methoxyindolin-2-one. 19.5 g (96%) of 1,3-dimethyl-3-γ-aminopropyl-5-methoxyindolin-2-one, with b.p. 167-170° at 1 mm was obtained. For analysis, the material with b.p. 168° at 1 mm was taken.

3.070 mg substance: 7.650 mg CO_2; 2.180 mg H_2O. 3.095 mg substance: 7.690 mg CO_2; 2.220 mg H_2O. 2.175 mg substance: 0.221 ml N_2 (23°, 726 mm). 2.790 mg substance: 0.279 ml N_2 (22°, 727 mm). Found %: C 67.95, 67.75; H 7.94, 8.00; N 11.19, 11.07. $C_{14}H_{20}O_2N_2$. Calculated %: C 67.70; H 8.12; N 11.28.

Picrate formed by combining alcoholic solutions of the base and picric acid crystallized from aqueous methanol in the form of yellow needles with m.p. 162-163°.

2.405 mg substance: 0.372 ml N_2 (25°, 730 mm). 3.185 mg substance: 0.490 ml N_2 (25°, 730 mm). Found %: N 17.10, 16.92. $C_{20}H_{25}O_9N_5$. Calculated %: N 17.11

Hydrogen iodide salt was obtained by addition of an alcoholic solution of hydrogen iodide to an alcohol-ether solution of the base. After crystallization from absolute alcohol, it was in the form of colorless crystals with m.p. 185.5-186.0°.

2.895 mg substance: 4.770 mg CO_2; 1.470 mg H_2O. 3.025 mg substance: 4.930 mg CO_2; 1.600 mg H_2O. 3.675 mg substance: 0.245 ml N_2 (23°, 747 mm). 3.715 mg substance: 0.245 ml N_2 (23°, 748 mm). Found %: C 44.93, 44.44; H 5.68, 5.92; N 7.56, 7.48. $C_{14}H_{21}O_2N_2I$. Calculated %: C 44.68; H 5.63; N 7.44.

8) 1,3-Dimethyl-3-γ-dimethylaminopropyl-5-methoxyindolin-2-one (dehydrohomoeseromeiolmethine) (VII). A solution of 19.5 g of 1,3-dimethyl-3-γ-aminopropyl-5-methoxyindolin-2-one in 18 ml of 40% aqueous formaldehyde solution with 20 ml of 90% formic acid was heated for 6 hours on a metal bath at 115-120°. Upon further treatment, as described in Procedure A for the synthesis of 1,3-dimethyl-3-β-dimethylaminoethyl-5-methoxyindolin-2-one, there resulted 17.7 g (82%) of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-methoxyindolin-2-one, with b.p. 162-164° at 2 mm.

3.045 mg substance: 7.815 mg CO_2; 2.395 mg H_2O. 3.035 mg substance: 7.710 mg CO_2; 2.390 mg H_2O. 2.820 mg substance: 0.255 ml N_2 (25°, 754 mm). 2.805 mg substance: 0.255 ml N_2 (24°, 741 mm). Found %: C 69.99, 69.27; H 8.80, 8.82; N 10.28, 10.19. $C_{16}H_{24}O_2N_2$. Calculated %: C 69.52; H 8.76; N 10.14.

Picrate, obtained in the usual manner, was obtained as yellow crystals, m.p. 139-140° after recrystallization from alcohol.

The hydrogen iodide derivative from alcoholic solutions of the base and hydrogen iodide. It crystallized from absolute alcohol in the form of colorless crystals with m.p. 181.0-181.5°; a mixture with hydrogen iodide salt of 1,3-dimethyl-3-γ-aminopropyl-5-methoxyindolin-2-one melted at 153-156°.

3.640 mg substance: 0.216 ml N_2 (21°, 747 mm). 3.500 mg substance: 0.225 ml N_2 (22°, 733 mm). Found %: N 6.74, 7.17. $C_{16}H_{25}O_2N_2I$. Calculated %: N 6.94.

9) 1,3-Dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one (dehydrohomoeserolinmethine) (IX). A solution of 15.0 g of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-methoxyindolin-2-one in 75 ml of 50% hydrobromic acid was heated for 2 hours on a metal bath at 140-145°, the reaction mixture then evaporated on a water bath, and the residue dissolved in a small volume of 20% potassium hydroxide solution. The solution was clarified by addition of 40% sodium bisulfite solution, and then made weakly alkaline to litmus paper. The base was extracted with butyl alcohol, the extract washed with water, and the butanol distilled off completely in vacuo. The residue upon grinding with ether crystallized. It was filtered by suction, washed with methanol and ether mixture, and recrystallized from methyl alcohol. 7.4 g (52%) of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one resulted – colorless crystals with m.p. 145-147°. After a second recrystallization, the substance had an m.p. of 147-148°.

2.980 mg substance: 7.505 mg CO_2; 2.245 mg H_2O. 3.090 mg substance: 7.800 mg CO_2; 2.330 mg H_2O. 3.020 mg substance: 0.294 ml N_2 (23°, 720 mm). 2.885 mg substance: 0.274 ml N_2 (25°, 730 mm). Found %: C 68.68, 68.83; H 8.43, 8.44; N 10.63, 10.45. $C_{15}H_{22}O_2N_2$. Calculated %: C 68.66; H 8.46; N 10.68.

Picrate was obtained by means of alcoholic picric acid, and recrystallized from alcohol – yellow needles with m.p. 184.5-185.0°.

The hydrogen iodide salt was obtained by mixing alcoholic solutions of the base and of hydrogen iodide, followed by precipitation with ether. After recrystallization from absolute alcohol, it represented colorless crystals with m.p. 192-193°; its mixture with the hydrogen iodide salt of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-methoxy ndolin-2-one had an m.p. of 160-162°.

3.050 mg substance: 5.130 mg CO_2; 1.585 mg H_2O. 3.005 mg substance: 5.090 mg CO_2; 1.630 mg H_2O. 3.370 mg substance: 0.215 ml N_2 (25°, 745 mm). 3.635 mg substance: 0.235 ml N_2 (25°, 745 mm). Found %: C 45.90, 46.19; H 5.81, 6.06; N 7.16, 7.26. $C_{15}H_{23}O_2N_2I$. Calculated %: C 46.16; H 5.94; N 7.17.

10) Dimethylcarbamic ester of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one (dimethylurethane of dehydrohomoeserolinmethine) (XI). The phenolate was prepared from 3.27 g (1.00 mole) of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one and 0.667 g (0.99 mole) of CH_3ONa in 15 ml of absolute methyl alcohol, which was then suspended in 35 ml of absolute benzene and treated with 2.00 g (1.49 moles) of dimethylcarbamic acid chloroanhydride. Reaction and isolation of the compound was carried out by a method described for synthesis of the dimethylurethane of dehydroeserolinmethine. There resulted 0.6 g of a darkening substance which melted in the air, and which was not investigated further, plus 3.60 g of 5-hydroxyindolin-2-one, with m.p. 103-105°.

3.045 mg substance: 0.314 ml N_2 (25°, 736 mm). 3.345 mg substance: 0.353 ml N_2 (23°, 735 mm). Found %: N 11.43, 11.78. $C_{18}H_{28}O_3N_3Cl$. Calculated %: N 11.35.

The picrate was obtained from an alcoholic solution of the hydrochloride and picric acid; it crystallized from alcohol in the form of yellow crystals with m.p. 134-135°.

SUMMARY

Synthesis of hydroxyindolic analogs of the alkaloid eserine, has been achieved – dimethylcarbamic esters of 1,3-dimethyl-3-β-dimethylaminoethyl-5-hydroxyindolin-2-one and of 1,3-dimethyl-3-γ-dimethylaminopropyl-5-hydroxyindolin-2-one.

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A CATALYTIC METHOD FOR SYNTHESIS OF α-METHYLNAPHTHALENE FROM α-CHLOROMETHYLNAPHTHALENE

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The isolation of α-methylnaphthalene from hard coal tar without impurities, offers great difficulties [1], and so, in those cases where pure α-methylnaphthalene is required, organic synthetic methods are used. The simplest of methods for α-methylnaphthalene can be considered to be the reduction of α-chloromethylnaphthalene, which can be carried out both catalytically and non-catalytically.

Of the non-catalytic methods to be found in the literature, reduction by means of zinc and hydrochloric acid is to be recommended [2], the yield of α-methylnaphthalene reaching 68%, but this method is applicable only for work with small quantities [3]. The literature contains only brief directions for catalytic procedures for reducing α-chloromethylnaphthalene. Vavon [4], in studying the synthesis of aromatic chloromethylated compounds, among them α-chloromethylnaphthalene, indicated the possibility of reducing them to the corresponding hydrocarbon by the use of hydrogen in the presence of platinum black. The yield of hydrocarbons reached 90-95%. Other investigators have described [5] the catalytic reduction of α-chloromethylnaphthalene in the presence of palladium on strontium carbonate. To tie up the hydrogen chloride evolving during reaction, sodium alcoholate was added. As a result, impure α-methylnaphthalene was obtained; the authors assume that it also contained α-naphthylcarbinol.

In the present work on hydrogenation of α-chloromethylnaphthalene, Raney nickel catalyst or palladium black was used; the reaction was studied in greater detail with nickel catalyst, and in this case hydrogenation was carried out under a variety of conditions. Hydrogenation experiments carried out without addition of a substance to neutralize the hydrogen chloride did not produce positive results because absorption of hydrogen rapidly ceased due to poisoning of the catalyst. Upon carrying out the reaction in presence of alkali in alcholic solution, regardless of whether pressure was used or not, there was also formed in addition to α-methylnaphthalene, the ethyl ester of α-naphthylcarbinol of di(α-naphthyl)-ethane.

$$\alpha\text{-}C_{10}H_7CH_2Cl \rightleftharpoons \begin{cases} \alpha\text{-}C_{10}H_7CH_2OC_2H_5 \\ \alpha\text{-}C_{10}H_7CH_3 \\ \alpha\text{-}C_{10}H_7CH_2CH_2C_{10}H_7\text{-}\alpha \end{cases}$$

Inasmuch as formation of the ethyl ester of α-naphthylcarbinol might be explained as due to the effect of alcoholic alkali, in place of alkali, anhydrous sodium acetate in alcoholic solution was used. As the result, under these conditions formation of the ethyl ester of α-naphthyl carbinol was either not observed at all, or it proceeded to a very minor degree. The yield of α-methylnaphthalene amounted to 85% of theory. Di-(α-naphthyl)-ethane was found to be a constant companion in the reaction, but its amount was small. The hydrogenation reaction was more convenient to carry out under elevated pressure. The inconvenience of the method was the low solubility of anhydrous sodium acetate in 96% ethyl alcohol, because of which the authors set up experiments on hydrogenation of α-chloromethylnaphthalene in the presence of alcoholic alkali and ethyl acetate. Thus, homogeneity of the medium was attained, and excess alkalinity removed rapidly by progressive hydrolysis of the ethyl acetate to form sodium acetate. Under these conditions, the yield of α-methylnaphthalene amounts to 85-87% of theory. In none of these cases was formation of the ethyl ester of α-naphthylcarbinol observed. The only by-product of the reaction was found to be the di-(α-naphthyl)-ethane. The same results were obtained by hydrogenation of α-chloromethylnaphthalene in the presence of palladium black, alcoholic alkali and ethyl acetate under atmospheric pressure. By hydrogenating α-chloromethylnaphthalene in the presence of sodium acetate or in a medium of ethyl acetate in alcoholic alkali, it was possible to obtain in the laboratory α-methylnaphthalene in any desired amount. The same method is adaptable to larger scale production. However, the question of the reaction course in the presence of alkali in a solution which consists of ethyl alcohol and ethyl acetate mixed, and the role of ethyl acetate requires a more extensive and thorough study.

EXPERIMENTAL

1. Hydrogenation of α-Chloromethylnaphthalene in the Presence of Nickel Catalyst and in Alcoholic Alkali

a) At atmospheric pressure. 17.3 g of α-chloromethylnaphthalene in 200 ml of alcoholic alkali and 10 g of catalyst in 20 ml of 96 % ethyl alcohol, were shaken in a hydrogen medium. After completion of absorption of the theoretical amount of hydrogen, the solution was filtered and the alcohol distilled off. The substance remaining was dissolved in ether, the ether solution washed with water, and dried with sodium sulfate. After distilling off the ether, the substance was distilled in vacuo.

α-Methylnaphthalene with b.p. 110-113° at 9 mm, resulted in the amount of 8.3 g (59 %), (picrate m. p. 141-141.5°); 9.5 g (34 %) of a higher boiling fraction, and an oily residue which crystallized upon standing, also were obtained.

b) Under elevated pressure. A solution of 50 g of α-chloromethylnaphthalene in alcoholic alkali (14.5 g of NaOH in 350 ml of ethyl alcohol) and 10 g of catalyst in 50 ml of alcohol were placed in an autoclave. The autoclave was filled with hydrogen to a pressure of 27.5 atm. Hydrogenation proceeded at room temperature with the autoclave rotating.

After completion of the reaction, and standard treatment, a substance was obtained which did not contain halogen (Beilstein test); it was distilled: 1st fraction, 98-110° at 6 mm – 26.9 g (67 %); 2nd fraction, b.p. 110-138° at 6 mm – 7.1 g. The residue in the flask, amounting to 2.3 g, crystallized. Upon repetition of the distillation, the following fractions were isolated:

1st: a substance with b.p. 96-103° at 5 mm, representing α-methylnaphthalene; picrate m.p. 142°. To determine the molecular refraction of α-methylnaphthalene, the substance which boiled at 96-103° at 5 mm was distilled over sodium; b.p. 97-98° at 5.5 mm; d_4^{20} 1.0187; n_D^{20} 1.6170; MR_D 48.83; calculated 49.07.*

2nd: a substance with b.p. 130-135° at 5.5 mm, representing the ethyl ester of α-naphthyl carbinol.

Di-(α-naphthyl)-ethane. There resulted from the residue which remained in the flask after the first distillation of substance (2.3 g) and washing with benzene, a white crystalline substance, which was soluble in benzene on heating, insoluble in alcohol, m.p. 155-158°; after two recrystallizations from benzene, the substance melted at 164°. Melting point, solubility and analytical data indicated that this substance was di-(α-naphthyl)-ethane.

Found %: C 93.40, 93.67; H 6.46, 6.39. $C_{22}H_{18}$. Calculated %: C 93.56; H 6.44.

Ethyl Ester of α-Naphthyl-carbinol. The higher fraction with b.p. 100-140° at 6-7 mm was distilled in vacuo, and the substance with b.p. 133-136° at 6.7 mm was taken, which was again distilled in vacuo; b.p. was 134-136° at 6 mm.**

Found %: C 83.52, 83.89; H 7.67, 7.57; OC_2H_5 23.84, 23.92. $C_{10}H_7CH_2OC_2H_5$. Calculated %: C 83.83; H 7.57; OC_2H_5 24.19.

2. Hydrogenation of α-Chloromethylnaphthalene in the presence of Nickel catalyst and of anhydrous sodium acetate.***

a) At atmospheric pressure. 10 g of α-chloromethylnaphthalene, an alcoholic solution of anhydrous**** sodium acetate (7.3 g CH_3COONa in 100 ml of 96 % alcohol) containing some undissolved sodium acetate, and 10 g of nickel catalyst, were hydrogenated by standard procedure.

After completion of hydrogen absorption and separation of the catalyst, the solution showed a weakly-alkaline reaction to litmus paper. After the usual treatment, 6.3 g (78.7 %) of α-methylnaphthalene with b.p. 128° at 28 mm, and 0.9 g of di-(α-naphthyl)-ethane residue which crystallized in the distilling flask, were obtained.

b) With elevated pressure. A solution of 50 g of α-chloromethylnaphthalene and 25 g of anhydrous sodium acetate in 500 ml of ethyl alcohol were placed in the autoclave and 10 g of nickel catalyst in 20 ml of alcohol added. The autoclave was filled with hydrogen to 28 atmospheres. Hydrogenation was continued for about one hour. After the usual treatment, a substance was obtained in the form of an oil, which did not

* The refraction was calculated, taking into account exaltation = 2.8.

** According to the literature data [6], b.p. is 144.5° at 11 mm.

*** Investigation by T. S. Safonova.

**** It was determined by the authors that use of ordinary sodium acetate complicated processing of the reaction product, as a result of which, the yield of α-methylnaphthalene was decreased.

contain halogen, The substance was distilled in vacuo. α-Methylnaphthalene distilled at 104° at 10 mm, 34.1 g (85%) resulting; 5.2 g of a higher-boiling residue was left behind in the flask, upon distillation of which 3.25 g of substance with b.p. 180-185° at 28 mm, or 134-135° at 6 mm (the ethyl ester of α-naphthylcarbinol) resulted, along with 0.97 g of a rapidly crystallizing residue, m.p. 162° (from benzene) [di-(α-naphthyl)-ethane].

3. Hydrogenation of α-Chloromethylnaphthalene in the Presence of Nickel Catalyst, Alcoholic Alkali and Ethyl Acetate.

a) At atmospheric pressure. 10 g of α-chloromethylnaphthalene, 15 ml of ethyl acetate, 100 ml of alcoholic alkali (3.7 g of sodium hydroxide in 100 ml of 96% alcohol), and 10 g of nickel catalyst were taken for reaction. Hydrogenation was carried out as usual. After completion of reaction, the solution showed a weakly alkaline reaction to litmus. 6.9 g of α-methylnaphthalene (86.2% of theory), b.p. 126-128° at 28 mm and 1 g of di-(α-naphthyl)-ethane, m.p. 162° (from benzene) resulted.

b) At elevated pressure. A solution of 50 g α-chloromethylnaphthalene in alcoholic alkali (18.5 g of NaOH in 450 ml of 96% ethyl alcohol) and 75 ml of ethyl acetate were placed in an autoclave, whereupon 10 g of catalyst in 20 ml of alcohol was introduced. Hydrogenation was carried out as usual at 28 atm. pressure. After completion of the reaction, the filtrate showed an acid reaction to litmus, neutral to Congo red.

33.9 g of α-methylnaphthalene with b.p. 96° at 5 mm (85%) resulted, and a crystalline substance with m.p. 156-158°. After crystallization from benzene, m.p. was 164°.

4. Hydrogenation of α-Chloromethylnaphthalene in the Presence of Palladium Black, Alcoholic Alkali and Ethyl Acetate.

2 g of palladium chloride was dissolved in a small amount of water, 10-15 ml of alcohol added, and the palladium chloride reduced by hydrogen to form palladium black. The liquid was poured off from the resulting palladium black into a beaker containing 20 g of α-chloromethylnaphthalene dissolved in a mixture of 30 ml ethyl acetate and 200 ml alcoholic alkali (7.2 g of NaOH and 200 ml of 80% ethyl alcohol).

13.5 g of α-methylnaphthalene (84.4 %) was obtained. B.p. 95-97° at 5 mm.

SUMMARY

1. By hydrogenation of α-chloromethylnaphthalene in the presence of Raney nickel and alcoholic alkali, the following are formed: α-methylnaphthalene (60-70%), the ethyl ester of α-naphthylcarbinol and di(α-naphthyl)-ethane.

2. By hydrogenation of α-chloromethylnaphthalene in alcoholic medium in the presence of Raney nickel and anhydrous sodium acetate, α-methylnaphthalene results in about 85% yield.

3. α-Methylnaphthalene results in 85-87% yield by hydrogenation of α-chloro-methylnaphthalene in the presence of catalyst (Raney nickel or palladium black), alcoholic alkali and ethyl acetate.

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INTERACTION OF ANABASINE WITH ORGANIC ACIDS

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In the preceding work [1], the authors examined interaction of anabasine with mineral acids, and it was demonstrated that isolation of the salts in a crystalline form occurs only in organic solvents, the best of which was found to be acetone. Having taken on the problem of examining interaction of anabasine with acids of various types and concentrations, the authors in the present article give results for interaction of anabasine with organic acids.

EXPERIMENTAL

Anabasine obtained from technical anabasine sulfate had n_D^{20} 1.5440 b.p. 106-110° at 4 mm.

All salts were analyzed for their acids content, which, for a majority of cases, was determined by conductometric titration with alkali hydroxide by the visual apparatus of A. P. Toropov [2]. Nitrogen was determined in stable, non-hygroscopic salts according to Dumas.

Synthesis and analysis of hygroscopic salts was carried out in a special apparatus in which the compound was completely isolated from the surrounding atmosphere [3].

The acid used for the work was purified and dehydrated beforehand.

Synthesis of Anabasine Formate. The compound resulted from direct mixing of anabasine and the acid in equimolecular quantities. Reaction proceeded with evolution of heat, and led to the formation of a thick, viscous mass, from which it was difficult to induce crystallization of the compound. The mass which crystallized was washed with gasoline or benzene, as the result of which it again converted to a thick mass, which again crystallized upon standing over calcium chloride in a desiccator. The crystals which formed melted in air, but again separated over calcium chloride. The resulting compound was very hygroscopic, darkening in air, a white crystalline compound, readily soluble in water, alcohol, ether and acetone. It was not possible to recrystallize it from these solvents because of its high solubility.

0.0356 g sub.: 2.3 ml 0.07548 N $Ba(OH)_2$. 0.0265 g sub.: 1.7 ml 0.07548 N $Ba(OH)_2$. Found %: HCOOH 22.45, 22.29. $C_{10}H_{14}N_2 \cdot HCOOH$. Calculated %: HCOOH 22.37.

Synthesis of Anabasine Acetate. As in the preceding case, upon mixing equimolecular quantities of anabasine and acetic acid, strong heat evolution resulted, and a thick, viscous mass formed, which after standing 24 hours, crystallized. The white crystals, washed with acetone, were dried in a vacuum desiccator, after which they possessed an m.p. of 88°. The resulting salt was hygroscopic.

0.0362 g sub.: 2.15 ml 0.07548 N $Ba(OH)_2$. 0.0310 g sub.: 1.85 ml 0.07548 N Ba(OH)2. Found %: CH_3COOH 26.92, 27.11. $C_{10}H_{14}N_2 \cdot CH_3COOH$. Calculated %: CH_3COOH 27.00.

Synthesis of Anabasine Butyrate. Anabasine butyrate also resulted with considerable heat evolution on interaction of equimolecular quantities of acid and anabasine. The resulting light-brown viscous mass crystallized after 24 hours. Upon washing the resulting crystals with gasoline or benzene, they converted into an oily liquid, yellow in color, which, upon standing over calcium chloride, again solidified in the form of white crystals. The resulting salt was very hygroscopic and difficult to wash free of impurities. It failed to crystallize out from available solvents.

0.0522 g sub.: 2.8 ml 0.07548 N $Ba(OH)_2$. 0.0444 g sub.: 2.3 ml 0.07548 N $Ba(OH)_2$. Found %: C_3H_7COOH 34.48, 35.67. $C_{10}H_{14}N_2 \cdot C_3H_7COOH$. Calculated %: C_3H_7COOH 35.19.

Synthesis of Anabasine Isovalerate. The compound resulted by direct interaction of equimolecular quantities of anabasine and acid. After 24 hours a solid compound was isolated from the solidified mass, which failed to recrystallize. After washing out the impurities with benzene, the crystals converted to a yellowish oily liquid from which, after standing in a desiccator over calcium chloride, it separated as white hygroscopic crystals.

0.0496 g sub.: 1.8 ml 0.1026 N KOH. 0.0722 g sub.: 2.7 ml 0.1026 N KOH. Found %: iso-C_4H_9COOH 38.01, 39.17. $C_{10}H_{14}N_2 \cdot C_4H_9COOH$. Calculated %: C_4H_9COOH 38.63.

Synthesis of Anabasine Oxalate. The oxalate was obtained from an acetone solution of anabasine and the anhydrous acid. Upon mixing the acetone solution, depending upon the ratio of acid to anabasine, three different types of salts separated: $2C_{10}H_{14}N_2 \cdot H_2C_2O_4$ with b.p. 210°, $C_{10}H_{14}N_2 \cdot H_2C_2O_4$ with b.p. 199° and $C_{10}H_{14}N_2 \cdot 2H_2C_2O_4$ with b.p. 81°. All three compounds were white substances, stable in air, readily soluble in water and poorly soluble in organic solvents. Prior to analyses, the salts were filtered by suction on a filter, washed thoroughly with acetone, and then dried in the air. The oxalic acid content in the compound was determined by titration with permanganate solution.

0.1300 g sub.: 15.3 ml N_2 (15°, 732 mm). 0.2408 g sub.: 28.5 ml N_2 (15°, 732 mm). 0.190 g sub.: 1.5 ml 0.0611 N $KMnO_4$. 0.0037 g sub.: 0.3 ml 0.0588 N $KMnO_4$. Found %: N 13.2, 13.27; C_2O_4 21.22, 21.00. $2C_{10}H_{14}N_2 \cdot C_2H_2O_4$. Calculated %: N 13.52; C_2O_4 21.23.

0.0079 g sub.: 0.85 ml N_2 (29°, 723 mm). 0.0139 g sub.: 1.5 ml N_2 (28°, 723 mm). 0.0050 g sub.: 0.25 ml 0.1540 N $KMnO_4$. 0.0040 g sub.: 0.50 ml 0.0610 N $KMnO_4$. Found %: N 11.10, 11.19; C_2O_4 33.88, 33.61. $C_{10}H_{14}N_2 \cdot C_2H_2O_4$. Calculated %: N 11.11; C_2O_4 34.09.

0.3412 g sub.: 26.8 ml N_2 (21°, 728 mm). 0.3417 g sub.: 26.5 ml N_2 (22°, 727 mm). 0.0702 g sub.: 5.3 ml 0.1540 N $KMnO_4$. 0.0276 g sub.: 5.5 ml 0.0588 N $KMnO_4$. Found %: N 8.52, 8.35; C_2O_4 51.18, 51.58. $C_{10}H_{14}N_2 \cdot 2C_2H_2O_4$. Calculated %: N 8.19; C_2O_4 51.42.

Synthesis of Anabasine Malonate. Upon mixing solutions of anabasine and malonic acid, a white crystalline compound separated, readily soluble in water and acetone. The salt was washed with benzene and dried over calcium chloride in a desiccator. M.p. 66°.

0.0159 g sub.: 0.97 ml 0.07548 N $Ba(OH)_2$. 0.0118 g sub.: 0.73 ml 0.07548 N $Ba(OH)_2$. Found %: $C_3H_4O_4$ 23.95, 24.29. $2C_{10}H_{14}N_2 \cdot C_3H_4O_4$. Calculated %: $C_3H_4O_4$ 24.28.

Synthesis of Anabasine Succinate. Upon mixing acetone solutions of succinic acid and anabasine in the ratio 1:2, a white crystalline compound precipitated. It was hygroscopic and melted readily in the air; its synthesis, therefore, and its analysis, were carried out in a special apparatus.

0.0231 g sub.: 1.4 ml 0.07548 N $Ba(OH)_2$. 0.0576 g sub.: 3.4 ml 0.07548 N $Ba(OH)_2$. Found %: $C_4H_6O_4$ 27.01, 26.30. $2C_{10}H_{14}N_2 \cdot C_4H_6O_4$. Calculated %: $C_4H_6O_4$ 26.67.

Synthesis of Anabasine Tartrate. As the result of mixing equimolecular quantities of d-tartaric acid and anabasine, there resulted from the viscous mass produced, after 24 hours standing, a precipitate, stable in air, white and crystalline. It was washed with acetone and dried in air, whereupon the m.p. was 115°.

0.5488 g sub.: 42.7 ml N_2 (26°, 723 mm). 0.0756 g sub.: 6.7 ml N_2 (29°, 724 mm). 0.0626 g sub.: 0.90 ml 0.4420 N $Ba(OH)_2$. 0.0429 g sub.: 0.62 ml 0.4420 N $Ba(OH)_2$. Found %: N 8.16, 9.05; $C_4H_6O_6$ 47.66, 47.92. $C_{10}H_{14}N_2 \cdot C_4H_6O_6$. Calculated %: N 8.97; $C_4H_6O_6$ 48.03.

Upon interacting d-tartaric acid with anabasine in acetone solution, a white solid of the composition, $2C_{10}H_{14}N_2 \cdot H_2C_4H_4O_6$.

0.2869 g sub.: 15.7 ml 0.07548 N $Ba(OH)_2$. 0.0309 g sub.: 1.75 ml 0.07548 N $Ba(OH)_2$. Found %: $C_4H_6O_6$ 30.98, 32.07. $2C_{10}H_{14}N_2 \cdot C_4H_6O_6$. Calculated %: $C_4H_6O_6$ 31.61.

Synthesis of Anabasine Citrate. This salt was prepared by mixing acetone solutions of anabasine and citric acid in a 3:1 ratio. The white flaky compound which precipitated was hygroscopic, melting readily in air, and readily soluble in water; it was therefore, prepared in a special apparatus, washed with acetone and after drying in vacuo was analyzed.

0.0968 g sub.: 5.8 ml 0.07548 N $Ba(OH)_2$. 0.0387 g sub.: 2.3 ml 0.07548 N $Ba(OH)_2$. Found %: $C_6H_8O_7$ 28.96, 28.72. $3C_{10}H_{14}N_2 \cdot C_6H_8O_7$. Calculated %: $C_6H_8O_7$ 28.29.

Synthesis of Anabasine β-Naphthalenesulfonate. Upon mixing acetone solutions of the acid and anabasine, in a one-to-one ratio, two compounds were isolated, of the following composition: $C_{10}H_{14}N_2 \cdot C_{10}H_7SO_3H$ with b.p. 139° and $C_{10}H_{14}N_2 \cdot 2C_{10}H_7SO_3H$ with b.p. 121°. The first salt resulted from a slight excess of anabasine, and the second by small acid excess. Both salts turned out to be crystalline compounds, stable in air, readily soluble in water and in excess acid.

0.0475 g sub.: 3.6 ml N_2 (29°, 721 mm). 0.0500 g sub.: 3.8 ml N_2 (30°, 721 mm). 0.0570 g sub.: 0.35 ml 0.4420 N $Ba(OH)_2$. 0.0460 g sub.: 0.28 ml 0.4420 N $Ba(OH)_2$. Found %: N 7.80, 7.84; $C_{10}H_7SO_3H$ 56.50, 56.40. $C_{10}H_{14}N_2 \cdot C_{10}H_7SO_3H$. Calculated %: N 7.57; $C_{10}H_7SO_3H$ 56.87.

0.1365 g sub.: 6.2 ml N_2 (27°, 723 mm). 0.1379 g sub.: 6.4 ml N_2 (32°, 723 mm). 0.0384 g sub.: 0.236 ml 0.4420 N $Ba(OH)_2$. 0.0630 g sub.: 0.488 ml 0.4420 N $Ba(OH)_2$. Found %: N 4.74, 4.70; $C_{10}H_7SO_3H$ 71.20, 71.25. $C_{10}H_{14}N_2 \cdot 2C_{10}H_7SO_3H$. Calculated %: N 4.85; $C_{10}H_7SO_3H$ 71.96.

EVALUATION OF RESULTS

Anabasine salts with monobasic acids possess high hygroscopicity. It is apparently due to this fact that the anabasine compound with formic acid was not isolated in solid form when the anabasine-formic acid system was studied by methods of physico-chemical analysis [4].

Hygroscopicity of anabasine compounds with organic acids depends upon their composition and upon the nature of the acid. They all crystallize over $CaCl_2$ in a desiccator. The anabasine compound with sulfuric and phosphoric acids did not crystallize under the same conditions, a fact which should be attributed to hygroscopicity of the acids themselves.

Upon examining salts of the anabasine compound with organic acids, there can be observed a regular order in their melting points. If the melting points for anabasine salts of various types are compared with the same acid, then those salts with the highest melting points will be the ones in which anabasine plays a role of monoacidic base, for example, the salts of anabasine with oxalic and β-naphthalenesulfonic acid. When the anabasine acts as a diacidic base, salts of lower melting points are formed.

Salts of anabasine with acids were prepared in a majority of cases by the authors from acetone solutions, and with only a few acids, such as formic and acetic, were salts formed with anabasine by direct interaction. The capacity of acids to form salts with anabasine in acetone solution depends upon their strength [5]. A strong acid such as β-naphthalenesulfonic acid, or an acid of average strength —oxalic acid— in acetone solution with anabasine forms several stable compounds. Very weak acids —salicyclic and benzoic— do not form salts with anabasine in acetone solution.

SUMMARY

1. Equimolecular, hygroscopic compounds of anabasine with formic, acetic, butyric and isobutyric acids have been prepared.

2. Crystalline compounds of anabasine with oxalic acid, of the composition as follows: $2C_{10}H_{14}N_2 \cdot C_2H_2O_4$, $C_{10}H_{14}N_2 \cdot C_2H_2O_4$ and $C_{10}H_{14}N_2 \cdot 2C_2H_2O_4$, have been synthesized, with malonic acid $2C_{10}H_{14}N_2 \cdot C_3H_4O_4$ and with citric acid, of the composition $2C_{10}H_{14}N_2 \cdot C_4H_6O_4$.

3. An anabasine compound with tartaric acid of the composition $2C_{10}H_{14}N_2 \cdot C_4H_6O_6$ and $C_{10}H_{14}N_2 \cdot C_4H_6O_6$ has been obtained; and with citric acid, of the composition $3C_{10}H_{14}N_2 \cdot C_6H_8O_7$.

4. Crystalline compounds of anabasine with β-naphthalenesulfonic acid, of the composition $C_{10}H_{14}N_2 \cdot C_{10}H_7SO_3H$ and of the composition $C_{10}H_{14}N_2 \cdot 2C_{10}H_7SO_3H$ have been obtained.

5. It has been observed that compounds of anabasine with organic acids behave predominately as a monoacidic base.

6. It has been demonstrated that acetone is a better solvent for the synthesis of salts of anabasine with acids, and that the formation of crystalline compounds is in direct relation to the strengths of these acids in acetone.

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INTERACTION OF ANABASINE WITH INORGANIC ACIDS

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In an earlier published work [1] the authors demonstrated that the alkaloid, anabasine, can form salts with mineral acids, representing stable crystalline substances. Upon interacting anabasine with hydrogen chloride and nitric acid, equimolecular compounds were isolated in crystalline form, while anabasine has been found to be a diacidic base. In the present work, the authors have engaged the problem of clarifying the behavior of anabasine as a base when it reacts with inorganic acids of various strengths and types.

Anabasine used for the work was isolated from technical anabasine sulfate. The resulting anabasine boiled at 106-110° (4 mm), n_D^{20} 1.5440.

All stable salts were analyzed for nitrogen content and for acid content. Analysis for nitrogen was carried out according to Dumas. The quantity of acid in the salt was determined by conductometric titration with barium hydroxide by means of the visual apparatus of A. P. Toropov [2], or by potentiometric titration with silver nitrate. For hygroscopic salts which melted in the air, analysis was carried out in a special apparatus in which the substance was completely isolated from the surrounding medium [3].

EXPERIMENTAL

Synthesis of Anabasine Hydrobromide. The salt of anabasine and hydrogen bromide separated in the form of needle crystals upon mixing equimolecular acetone solutions of anabasine and hydrogen bromide, cooled in ice, and was purified by a procedure known in the literature [4]. The salt was stable in air, readily soluble in water and in excess hydrogen bromide. After thorough washing with acetone and drying, it had a m.p. of 181°. The salt could be recrystallized from acetone, which was difficult however, due to low solubility in this solvent.

Found %: N 11.40, 11.26; Br 32.26, 33.17. $C_{10}H_{14}N_2 \cdot HBr$. Calculated %: N 11.52; Br 32.86.

Synthesis of Anabasine Hydriodide. As in the preceding case, a compound of anabasine and hydriodic acid resulted upon mixing equimolecular quantities of anabasine and hydrogen iodide dissolved in acetone, cooled with ice. The hydrogen iodide was prepared and purified by a method known in the literature [4]. The anabasine hydriodide was in the form of a fine, white crystalline powder, stable in air and readily soluble in water and excess acid. Recrystallization of this salt from acetone was hindered because of its poor solubility. The salt thoroughly washed with acetone and dried in air had a m.p. of 253°.

Found %: N 9.23, 9.39; I 43.37, 43.44. $C_{10}H_{14}N_2 \cdot HI$. Calculated %: N 9.66; I 43.59.

It should be mentioned that the crystalline hydriodide, as well as the hydrobromide, separates only upon mixing cooled acetone solutions containing equimolecular quantities of anabasine and acid. At other ratios the crystalline compound failed to separate.

Synthesis of Anabasine Sulfate. If sulfuric acid is carefully added, with continuous stirring, to a solution of anabasine in acetone, then the anabasine sulfate separates in the form of white, crystalline flakes, dissolving in excess of acid. Upon filtering this salt in air, it becomes viscous because of hygroscopicity, and cannot be removed from the filter. However, upon isolating the substance from surrounding medium in a special apparatus, it was possible to isolate it and to analyze it. Anabasine sulfate resulted upon addition of sulfuric acid to an anabasine solution for the calculated ratio of 1:1. Upon interacting one acid molecule with two molecules of anabasine a yellow viscous mass separated. Because of its hygroscopicity, the anabasine sulfate was analyzed only for the acid content.

Found %: H_2SO_4 37.01, 36.93. $C_{10}H_{14}N_2 \cdot H_2SO_4$. Calculated %: H_2SO_4 37.68.

Synthesis of Anabasine Phosphate. Chemically-pure orthophosphoric acid was taken for synthesis of the salt. To a solution of the acid in acetone there was added anabasine. The white flakes which precipitated out at first converted to a white powder when stirred with a rod. The compound was so hygroscopic that upon filtration by suction, and repeated washing with acetone in a special apparatus, it melted rapidly. Analysis for the acid content only

was carried out, because of the extreme hygroscopicity of the salt. Several batches were taken for analysis, and each time a sample was taken from a freshly synthesized portion of salt.

Found %: H_3PO_4 16.96, 16.31. $3C_{10}H_{14}N_2 \cdot H_3PO_4$. Calculated %: H_3PO_4 16.76.

Data given in the present and in the preceding [1] articles indicate that monobasic inorganic acids form compounds with anabasine which are stable in air. They are all electrolytes and possess considerable electroconductivity. Anabasine sulfate and phosphate salts are highly hygroscopic. The examples considered also indicate that anabasine behaves predominately as a monoacidic base during interaction with inorganic acids, which leads to formation of the crystalline compound.

SUMMARY

1. A crystalline salt of anabasine with hydrogen bromide has been obtained, of the composition $C_{10}H_{15}N_2 \cdot HBr$.

2. A crystalline salt of anabasine with hydrogeniodide, of the composition $C_{10}H_{14}N_2 \cdot HI$ has been synthesized.

3. A solid hygroscopic salt of anabasine with sulfuric acid, of the composition $C_{10}H_{14}N_2 \cdot H_2SO_4$ has been synthesized.

4. A solid hygroscopic salt of anabasine with orthophosphoric acid, of the composition $3C_{10}H_{14}N_2 \cdot H_3PO_4$ has been obtained.

5. It has been demonstrated that anabasine, as crystalline salts with inorganic acids, behaves predominately as a monoacidic base.

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Central Asian State University

* See Consultants Bureau Translation, page 955.

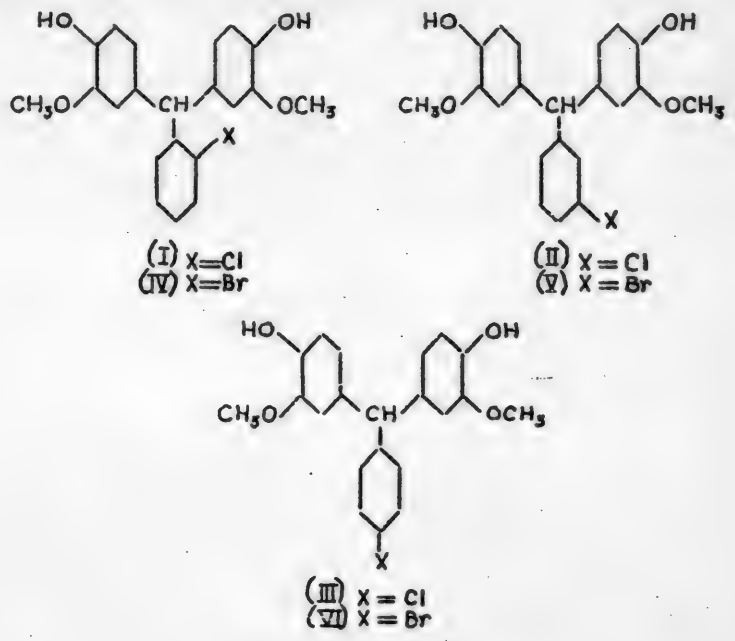
RESEARCH IN THE FIELD OF HYDROXYFUCHSONE DYES

XVIII. HALOGEN DERIVATIVES OF 3,3'-DIMETHOXYBENZAURIN

I. S. Ioffe and B. G. Belenky

Extending the work described in the preceding article [1], the authors have obtained halogen derivatives of 3,3'-dimethoxy-4'-hydroxyfuchsone, containing chlorine and bromine atoms in different positions of the phenyl ring.

The corresponding leuco derivatives (I–VI) were obtained by condensing isomeric chlorobenzaldehydes and bromobenzaldehydes with guaiacol in the presence of hydrogen chloride.



All of these triphenylmethane derivatives were obtained, after crystallization from alcohol or from acetic acid, in the form of colorless crystals, whose melting points are given in Table 1.

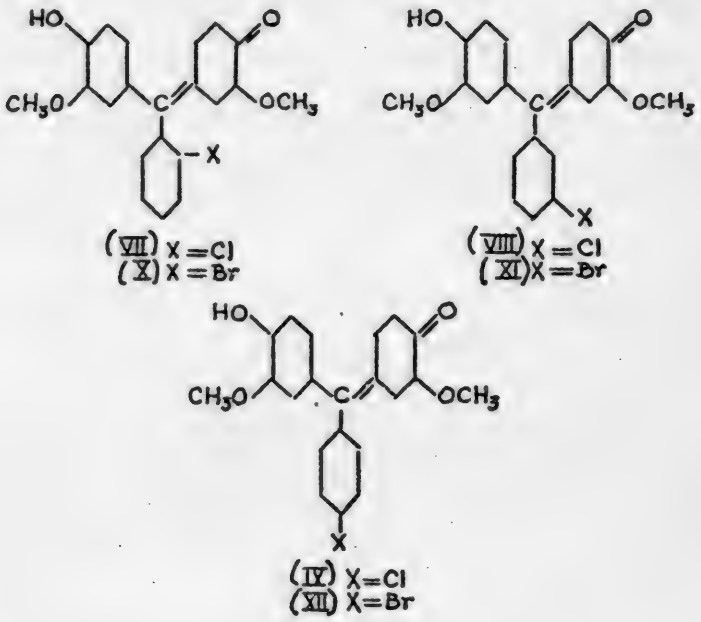
TABLE 1

No.	Name of compound	Melting point (in °C)
I	2''-Chloro-	120-130 (with decomposition)
II	3''-Chloro-	130-140 (with decomposition)
III	4''-Chloro	129-130
IV	2''-Bromo-	120-130 (with decomposition)
V	3''-Bromo-	120-130 (with decomposition)
VI	4''-Bromo-	126-127

(Name of compound: 3,3'-dimethoxy-4,4'-dihydroxytriphenylmethane)

It should be stressed that o- and m-halogen derivatives are unstable when heated above 100°, and are subject to some conversions that have not been studied up to the present time; the p-derivative, however, melted sharply within a 1° range.

By passing nitrogen oxides through solutions of all leuco derivatives, in amyl acetate saturated with hydrogen chloride, the authors obtained salts of the corresponding hydroxyfuchsone dyes (VII-XII):



These salts were hydrolyzed by water, converted into the hydrated forms of hydroxyfuchsones. Hydrolysis was more rapid in the presence of acetic acid salts. Upon boiling the hydrated forms with acetic acid, and distilling off the solvent in vacuo, there resulted the anhydrous forms of the dyes, which were purified by crystallization from dry benzene or from glacial acetic acid. Melting points of the halogen derivatives of 3,3'-dimethoxy-4'-hydroxyfuchsone are given in Table 2.

As can be seen from this work, the p-isomers have the highest melting points, and the m-isomers give the lowest.

TABLE 2

No.	Substance name		Melting point (in °C)
VII	2''-Chloro-	3,3'-dimethoxy-4-hydroxyfuchsone	164-166
VIII	3''-Chloro-		147-148
IX	4''-Chloro-		203
X	2''-Bromo		171-172
XI	3''-Bromo		143-144
XII	4''-Bromo		202-205

EXPERIMENTAL

I. Leuco Derivatives of the Dyes

0.05 mole of the aldehyde (7 g of chlorobenzaldehyde or 9.25 g of bromobenzaldehyde) was dissolved in a thick-walled beaker with 0.12 mole of molten guaiacol (15 g) and a stream of dry hydrogen chloride passed through the resulting mixture to saturation. After standing for one week in a hermetically-sealed vessel, the mixture solidified to a homogeneous crystalline monolith. The crude reaction product was treated with hot water and it then melted. After this procedure, the substance was heated several times with 100 ml of 10% soda solution until it became solid in boiling water. The yield of product purified in such fashion was faintly colored, gray-green in color, and varied in yield for individual leuco derivatives from 65-80% of theory. Such product was in itself suitable for further oxidation to the hydroxyfuchsone dye.

To obtain the leuco derivative in analytically-pure form, the product described above was flushed with a small volume of alcohol, which dissolved the impurities, and after filtration, the product was crystallized several times from alcohol or acetic acid.

Halogen was determined on the resulting compound (according to Stepanov). The analytical results are given in Table 3.

TABLE 3

No.	Formula	Batch (in g)	0.1 N $AgNO_3$* (in ml)	Halogen found (in %)	Halogen calculated (in %)
I	$C_{21}H_{19}O_4Cl$	0.2033, 0.2113	5.30, 5.55	9.25, 9.31	9.58
II	$C_{21}H_{19}O_4Cl$	0.2040, 0.1980	5.43, 5.30	9.45, 9.48	9.58
III	$C_{21}H_{19}O_4Cl$	0.2132, 0.2240	5.78, 5.95	9.62, 9.43	9.58
IV	$C_{21}H_{19}O_4Br$	0.2430, 0.2445	5.78, 5.90	19.00, 19.30	19.27
V	$C_{21}H_{19}O_4Br$	0.2135, 0.2110	5.15, 5.05	19.30, 19.13	19.27
VI	$C_{21}H_{19}O_4Br$	0.1998, 0.2018	4.75, 4.85	19.00, 19.21	19.27

II. Hydroxyfuchsone Dyes

A. Synthesis of the Dye Hydrochlorides. 5 g of the leuco derivative (crude condensation product washed free of guaiacol excess can be taken for the reaction) was dissolved in 50 ml of amyl acetate; the resulting solution was saturated with dry hydrogen chloride, and then, along with hydrogen chloride, a stream of nitrogen oxides containing nitrogen dioxide was passed in for 2 hours. Thereupon the dye hydrochloride formed a precipitate in the form of bronze flakes. After standing for 2 hours, the dye salt precipitate was filtered off, washed with amyl acetate to a colorless filtrate, and dried. The yield was approximately quantitative when pure leuco compound was used.

B. Synthesis of Hydroxyfuchsone. 5 g of the hydrochloride dye was gound in a mortar with 50 ml of acetic acid, and 50 ml of 25% potassium acetate solution added to the suspension, and the resulting mixture poured into 250 ml of water with stirring. Thereupon the hydroxyfuchsone dye precipitated in hydrated form as brick-red flakes, which were filtered, washed with water and dried in a vacuum desiccator. The resulting substance was dissolved with heating in 50 ml of glacial acetic acid, and the acetic acid, along with the water which separated from the hydrated form, was distilled off from the solution in vacuo. Ether was poured over the precipitate, filtered, dried in a desiccator. The resulting substance crystallized nicely from dry benzene or glacial acetic acid.

Properties of the hydroxyfuchsone synthesized are given in Table 4.

TABLE 4

No.	Halogen position	Crystal structure	Color of solution	
			in the acid	in alkali
VII	o-Cl	Orange-yellow platelets	Dark-purple	Blue-violet
VIII	m-Cl	Orange-red crystals	Violet	Blue
IX	p-Cl	Red prisms	Purple-red	Blue
X	o-Br	Yellow-orange platelets	Violet	Blue-violet
XI	m-Br	Red crystals	Purple	Blue-violet
XII	p-Br	Red crystals	Purple	Blue

For the dyes synthesized, halogen was determined according to Stepanov. Analytical data are given in Table 5.

TABLE 5

No.	Formula	Batch (in g)	0.1 N $AgNO_3$* (in ml)	Halogen found (in %)	Halogen calculated (in %)
VII	$C_{21}H_{17}O_4Cl$	0.2100, 0.2054	5.58 5.33	9.43, 9.22	9.64
VIII	$C_{21}H_{17}O_4Cl$	0.2213, 0.2210	5.85, 5.90	9.36, 9.49	9.64
IX	$C_{21}H_{17}O_4Cl$	0.1988, 0.1930	5.38, 5.23	9.61, 9.62	9.64
X	$C_{21}H_{17}O_4Br$	0.2045, 0.2130	4.88, 5.10	19.10, 19.15	19.35
XI	$C_{21}H_{17}O_4Br$	0.2320, 0.2450	5.53, 5.83	19.06, 19.03	19.35
XII	$C_{21}H_{17}O_4Br$	0.2240, 0.2276	5.33, 5.43	19.03, 19.10	19.35

* Quantity of $AgNO_3$ used for tying up halogen.

SUMMARY

By condensing isomeric chlorobenzaldehydes and bromobenzaldehydes with guaiacol, the corresponding triphenylmethane derivatives have been obtained, from which, by oxidation with nitrogen oxides in amyl acetate saturated with hydrogen chloride, the hydrochloride salts of the isomeric chloro- and bromo-derivatives of 3,3'-dimethoxy-4'-hydroxyfuchsone have been obtained. The free hydroxyfuchsone dyes have been obtained in analytically-pure form from the salts.

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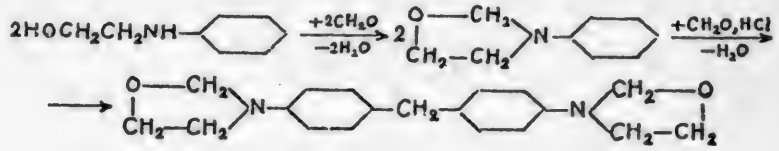
* See Consultants Bureau Translation, page 1597.

INTERACTION OF 3-PHENYLOXAZOLIDINE AND SOME OTHER OXAZILIDINE DERIVATIVES WITH FORMALDEHYDE

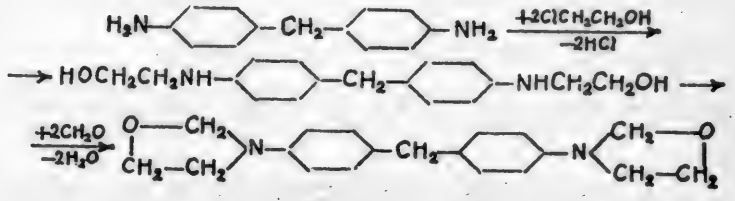
K. D. Petrov and O. K. Gosteva

The authors described earlier [1] the reaction of 3-phenyloxazolidine with formaldehyde, which takes place in the presence of hydrochloric acid, forming p,p'-di(oxazolidyl-3)-diphenylmethane. As new observations have indicated, it is more expedient to synthesize the same product from ethanolaniline and formaldehyde in alcoholic medium. The process in this case is carried out in such a manner that the 3-phenyloxazolidine (in the form of an oil layer) which is forming from the ethanolaniline and formaldehyde is dissolved by addition of alcohol, and condensed further with formaldehyde in the presence of hydrochloric acid to give p,p'-di(oxazolidyl-3)-diphenylmethane:



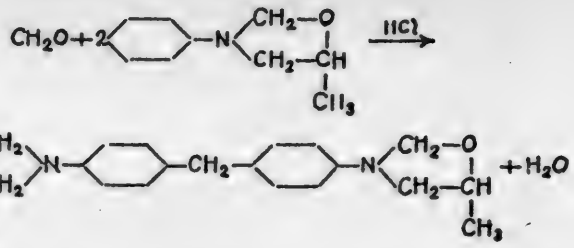
In this case the product resulted in purer form in about 80% yield. Its structure is conditioned by its mode of formation. It is generally known that N-alkylanilines condense with formaldehyde at the p-position, with formation of the corresponding diphenylmethane derivatives [2]. However, 3-phenyloxazolidine having in its structure the $-CH_2-\underset{|}{N}-CH_2-$, arrangement of atoms, is structurally close to that of N-alkylanilines. Hence its reaction with formaldehyde probably proceeds at the p-position, i.e., with formation of p,p'-di(oxazolidyl-3)diphenylmethane.

Moreover, the structure of p,p'-di(oxazolidyl-3)-diphenylmethane is confirmed by its synthesis from p,p'-diaminodiphenylmethane:



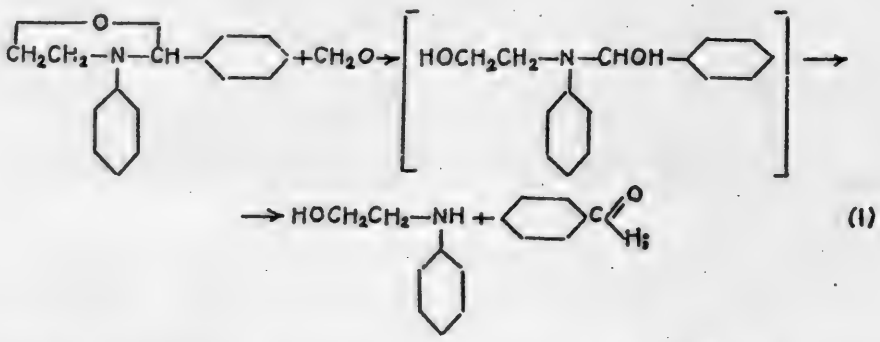
While carrying out this synthesis, p,p'-diethanoldiaminidiphenylmethane (intermediate product) failed to separate in the pure state due to the presence of resinous side-products in the reaction mixture. Therefore, in order to obtain the p,p'-di-(oxazolidyl-3)-diphenylmethane, the authors used crude p,p'-diethanoldiaminodiphenylmethane. For this purpose, the latter was mixed with formaldehyde and heated. The p,p'-di-(oxazolidyl-3)diphenylmethane melted at 141-142°, i.e., in the same range as the condensation product of 3-phenyloxazolidine with formaldehyde (m.p. 141-142°). A mixed sample also melted at 141-142°. Thus was confirmed the identity of these substances, and hence also the fact that reaction of 3-phenyloxazolidine with formaldehyde actually does proceed with formation of p,p'-di-(oxazolidyl-3)-diphenylmethane.

Apart from the above, the formaldehyde reaction with 3-phenyl-5-methyloxazolidine with 2,3-diphenyloxazolidine, and with 2-furyl-3-phenyloxazolidine, was also studied. Here reaction of 3-phenyl-5-methyloxazolidine with formaldehyde proceeded with formation of p,p'-di-(5-methyloxazolidyl-3)-diphenylmethane:

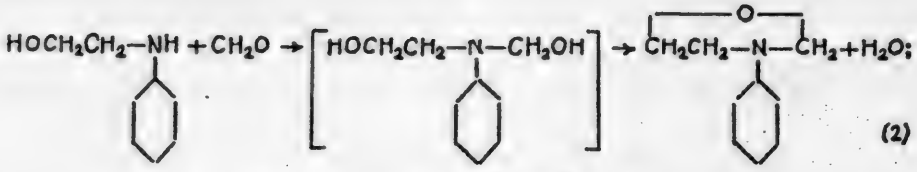


This was confirmed by analysis of the product obtained, and by determination of its molecular weight.

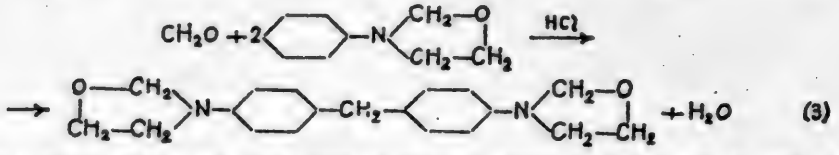
However, reaction of 2,3-diphenyloxazolidine and of 2-furyl-3-phenyloxazolidine with formaldehyde proceeds in another direction. Thus, for example, the reaction of 37% formalin with 2,3-diphenyloxazolidine in the presence of hydrochloric acid gave benzaldehyde and p,p'-(oxazolidyl-3-)diphenylmethane, instead of the expected p,p'-di-(2-phenyloxazolidyl-3)diphenylmethane. Formation of these compounds can be explained as follows:



(1)



(2)



(3)

Reaction of 2-furyl-3-phenyloxazolidine* with formaldehyde also proceeded along similar lines. When this reaction was carried out by the authors, only p,p'-di-(oxazolidyl-3)-diphenylmethane resulted. Furfural failed to separate from the reaction mass because of its resinification.

EXPERIMENTAL

(V. I. Pukhova participating)

1. Synthesis of p,p'-Di-(oxazolidyl-3)-diphenylmethane from Ethanolaniline and Formaldehyde. 3-Phenyloxazolidine was first prepared from ethanolaniline and formaldehyde by gradual addition of 411 g (3 moles) of ethanolaniline to 439 g of 36.9% formalin (5.4 moles CH_2O). The process was carried out with stirring, accompanied by spontaneous evolution of heat and formation of an oily layer of 3-phenyloxazolidine, which settled to the bottom of the container. After addition of all of the ethanolaniline, alcohol was added to the reaction mixture to the formation of a homogeneous, transparent solution – 950 ml. Then, 9 ml of hydrochloric acid (d 1.18) was added, with

* Synthesis of initial 2-furyl-3-phenyloxazolidine for carrying out this reaction is described in the experimental part. At the same time is also given synthesis for 2-furyl-3-phenyl-5-methyloxazolidine.

stirring, to the mixture. The resulting p,p'-di-(oxazolidyl-3)-diphenylmethane precipitated in the form of white scales. The crystals were filtered off on a Nutsch filter and dried at 95-100° to constant weight. The yield of p,p'-di-(oxazolidyl-3)-diphenylmethane was 360 g (77.40%). The resulting product melted at 136-137°; after recrystallization from alcohol, it melted in the range 141-142°. A sample mixed with known p,p'-di-(oxazolidyl-3)-diphenylmethane (see experiment 2) also melted at 141-142°. Identity of the resulting product with p,p'-di-(oxazolidyl-3)-diphenylmethane was confirmed by analysis.

0.2302 g sub.: 0.6208 g CO_2; 0.1466 g H_2O. 0.1782 g sub.: 0.4791 g CO_2; 0.1242 g H_2O. Found %: C 73.62, 73.39; H 7.13, 7.12. $C_{19}H_{22}O_2N_2$. Calculated %: C 73.50, H 7.09.

2. Synthesis of p,p'-di-(oxazolidyl-3)-diphenylmethane from diaminodiphenylmethane and ethylene chlorohydrin. The p,p'-diethanoldiaminodiphenylmethane was prepared first by heating on an oil bath 19.8 g (0.01 mole) of diaminodiphenylmethane with 17.7 g (0.22 mole) of ethylene chlorohydrin in the presence of 3 ml of water, according to Shorygin [3, 4]. Reaction was carried out with mechanical stirring. The reaction mixture solidified after 8 hours of heating. 50 ml of alcohol was added in order to dissolve it, and the reaction mass was then heated for another 8 hours. After completion of the process, the resulting product (p,p'-diethanoldiaminodiphenylmethane) was treated with saturated soda solution and was filtered on a Nutsch filter, and the filtrate then diluted with 50 ml of alcohol. The p,p'-diethanoldiaminodiphenylmethane could not be isolated by recrystallization from alcohol.

The alcoholic solution of crude p,p'-diethanoldiaminodiphenylmethane was mixed with 17.8 g of 37% formalin (0.22 mole of CH_2O) in order to synthesize the p,p'-di-(oxazolidyl-3)-diphenylmethane, heating being carried out on a water bath for 15 minutes at 50-60°. After standing for 24 hours, there separated from the reaction mixture at room temperature a white crystalline precipitate of p,p'-di-(oxazolidyl-3)-diphenylmethane. The resulting product was filtered by suction through a Nutsch filter and was purified by recrystallization from benzene, after which procedure it melted at 141-142°. There was obtained 4.6 g of pure substance.

0.3781, 0.7231 g sub.: 24.08, 45.63 ml 0.1 N H_2SO_4. Found %: N 8.91, 8.83. $C_{19}H_{22}O_2N_2$. Calculated %: N 9.03.

3. p,p'-Di-(5-methyloxazolidyl-3)-diphenylmethane. 40.8 g (0.25 mole) of 3-phenyl-5-methyloxazolidine was mixed with 61.4 g of 36.6% formalin (0.74 mole of CH_2O), 10 ml of dioxane, and 2 ml of hydrochloric acid (d 1.18). The reaction was carried out with mechanical stirring for 4 hours. A white crystalline product precipitated. After completion of the process, the reaction mixture was neutralized with soda solution. The crystals were aspirated off onto a Nutsch filter; they melted at 95-96°. 16 g of substance was obtained.

0.2674 g sub.: 0.7266 g CO_2; 0.1910 g H_2O. 0.6418 g sub.: 37.15 ml 0.1 N H_2SO_4. 0.1223 g sub.: 30.82 g of benzene: Δt: 0.06°. Found %: C 74.12; H 7.90; N 8.10; M 339. $C_{21}H_{26}O_2N_2$. Calculated %: C 74.56; H 7.69; N 8.28; M 338.

4. Interaction of 2,3-diphenyloxazolidine with formaldehyde. 11.3 g (0.05 mole) of 2,3-diphenyloxazolidine (concerning which preparation see [3, 5]) was mixed with 8 g of 37% formalin (0.098 mole CH_2O), 1 ml of hydrochloric acid (d 1.18) and 50 ml of dioxane. Reaction was continued for 18 hours with stirring until a white precipitate separated. The crystals were filtered off onto a Nutsch filter and washed with soda solution, followed by water. 5 g of crystals resulted. After two recrystallizations from alcohol, the product melted at 141-142°.

The mixture with a known sample of p,p'-di-(oxazolidyl-3)-diphenylmethane (m.p. 141-142°) melted in the same range, which confirmed the identity of these substances. According to the analytical data, the product resulting from this experiment also corresponded to p,p'-di-(oxazolidyl-3)-diphenylmethane.

0.1682 g sub.: 0.4549 g CO_2; 0.1128 g H_2O. Found %: C 73.73; H 7.50. $C_{19}H_{22}O_2N_2$. Calculated %: C 73.50; H 7.09.

In investigating the filtrate obtained by vacuum filtration of p,p'-di-(oxazolidyl-3)-diphenylmethane, the benzaldehyde failed to separate in sufficiently pure state, and the experiment had to be repeated. For this purpose, 60 g (0.27 mole) of 2,3-diphenyloxazolidine, 43.7 g of 36.6% formalin (0.54 mole CH_2O), 1 ml of hydrochloric acid (d 1.18) and 200 ml of dioxane were taken for reaction. 8.3 g of p,p'-di-(oxazolidyl-3)-diphenylmethane (m.p. 141-142°) was formed, along with 6.9 g of benzaldehyde, and separation of the benzaldehyde was carried out by fractionation of the filtrate after filtering off the p,p'-di-(oxazolidyl-3)-diphenylmethane with suction. Dioxane was first removed on the column at atmospheric pressure, and the residue, with a characteristic odor of benzaldehyde, was distilled from a Claisen flask at decreased pressure. In order to remove impurities from the resulting product it was then distilled for a second time at atmospheric pressure. The benzaldehyde was collected in the range 176-179° at 745 mm. 6.9 g was obtained; $n_D^{19.5}$ 1.5448; d_{20}^{20} 1.0455. Upon subsequent distillation of this fraction

the benzaldehyde was collected in a narrower range, 178-179° at 754 mm. 1.8 g resulted; $n_D^{19.5}$ 1.5455. The following constants are given in the literature [6] for benzaldehyde: b.p. 178.3 at 760 mm; 179.1° at 751.3 mm; $n_D^{19.5}$ 1.5456; d_{15}^{15} 1.0500; d_{25}^{25} 1.0434).

The resinous reaction products (distillation residues) which resulted from this experiment were not investigated further by the authors.

5. 2-Furyl-3-phenyloxazolidine was prepared by stirring 96 g (1 mole) of furfural with 137 g (1 mole) of ethanolaniline for 10 minutes in the presence of 1 g of potash, after which the reaction mixture was fractionated in vacuo. The 2-furyl-3-phenyl-oxazolidine fraction was collected in the range 165-171° at 7 mm. 137 g of substance resulted. Yield was 63.39% of theory. The resulting product externally resembled a yellow oil (darkening during a lapse of time):

d_{20}^{20} 1.1781; n_D^{20} 1.5855; MR_D 61.40; calculated 60.53.

0.3980 g sub.: 1.0594 g CO_2; 0.2270 g H_2O. 1.7724 g sub.: 25.54 g benzene: Δt 1.625°. Found %: C 72.60; H 6.38; M 219. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.04; M 215.

6. 2-Furyl-3-phenyl-5-methyloxazolidine. 151 g (1 mole) of β-hydroxypropylaniline was mixed with 105.68 g (1.1 moles) of freshly distilled furfural and 2 g of potash. The mixture was further distilled in vacuo. The 2-furyl-3-phenyl-5-methyloxazolidine fraction was collected in the range 130-135° at 1.5 mm. There resulted 165 g (72%) of substance. The product superficially resembled a thick, viscous, yellowish oil (darkening with time).

d_{20}^{20} 1.1334; n_D^{20} 1.5710; MR_D 66.07; calculated 65.14.

0.4382 g sub.: 1.1788 g CO_2; 0.2722 g H_2O. 0.7928 g sub.: 28.06 g benzene: Δt 0.63°. Found %: C 73.37; H 6.90; M 230. $C_{14}H_{15}O_2N$. Calculated %: C 73.36; H 6.35; M 229.

7. Interaction of 2-furyl-3-phenyloxazolidine with formaldehyde. 18.5 g (0.086 mole) of 2-furyl-3-phenyloxazolidine was mixed with 14 g of 37% formalin (0.172 mole CH_2O), 100 ml of alcohol and 0.5 ml of strong hydrochloric acid. Reaction was carried out for 18 hours, and processed as in the preceding case (see experiment 4), with formation of p,p'-di-(oxazolidyl-3)-diphenylmethane. After recrystallization from alcohol, 12 g of product with m.p. 141-142° resulted. A sample mixed with known sample of p,p'-di-(oxazolidyl-3)-diphenylmethane (see experiment 2) melted at the same temperature, indicating identity of these substances. The resinous reaction products obtained in this experiment were not investigated further.

SUMMARY

1. A method for synthesis of p,p'-di-(oxazolidyl-3)-diphenylmethane has been described.

2. Synthesis of p,p'-di-(5-methyloxazolidyl-3)-diphenylmethane, 2-furyl-3-phenyl-oxazolidine and 2-furyl-3-phenyl-5-methyloxazolidine, not described in the literature, has been given.

3. It has been established that, contrary to expectations, 2,3-diphenyloxazolidine reacts with formaldehyde to form p,p'-di-(oxazolidyl-3)-diphenylmethane and benzaldehyde. A reaction mechanism for this reaction has been given. It has been established that according to similar scheme 2-furyl-3-phenyloxazolidine reacts with formaldehyde.

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CATALYTIC CONVERSION OF 2,2-DIMETHYLFURANIDINE INTO 2,2-DIMETHYLTHIOPHANE AND INTO HYDROCARBONS. XLI.

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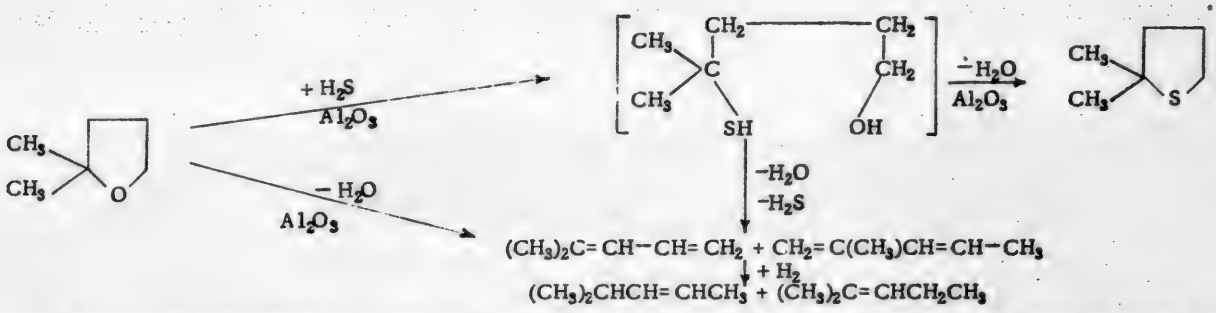
It was pointed out in the preceding article [1] that the principal factors which limit completeness of the conversion of furanidine homologs to the corresponding thiophane homologs are the number and types of alkyl groups bound to the furanidine ring, as well as their positions relative to the oxygen bridge of this ring. Whereas furanidine converts almost completely into thiophane, and 3,3-dimethylfuranidine into 3,3-dimethylthiophane [1], in yields (73%) approximating that for 3-methylthiophane as obtained from 3-methylfuranidine, the reaction of 2,2,5,5-tetraalkylfuranidines with hydrogen sulfide under catalytic conditions for conversion of heterocycles produce only mixtures of two unsaturated hydrocarbons with different double bond locations [2]. The formation of diene hydrocarbons in this case is conditioned by the simultaneous splitting out of water and hydrogen sulfide from the intermediate ditertiary 1,4-mercaptohydroxy compounds.

In its structure, 2,2-dimethylfuranidine lies between furanidine and 2,2,5,5-tetramethylfuranidine. It should, by adding hydrogen sulfide under the conditions of catalytic conversion of heterocycles, convert into the intermediate, primary, tertiary mercaptohydroxy compound $(CH_3)_2C(SH)CH_2CH_2CH_2OH$, which should be able to split out water and hydrogen sulfide to form the diene hydrocarbon, and to split out water, forming only the cyclic compound, 2,2-dimethylthiophane.

It has been determined in the present work that 2,2-dimethylfuranidine, when passed over aluminum oxide in a stream of hydrogen sulfide at 350°, does in fact produce 2,2-dimethylthiophane (yield 27%) and a mixture of unsaturated hydrocarbons. Catalytic dehydration of 2,2-dimethylfuranidine in the absence of hydrogen sulfide led to the formation of a hydrocarbon mixture which contained 2-methylpentadiene-1,3, 2-methylpentadiene-2,4, 2-methylpentene-2 and 2-methylpentene-3.



Formation of ethylenic hydrocarbons is explained by reduction of diene hydrocarbons with hydrogen which appears in the reaction zone as the result of destructive processes.

EXPERIMENTAL

2,2-Dimethylfuranidine. Acetopropyl alcohol (25 g) was added to an ether solution of methylmagnesium iodide (from 12 g of Mg and 75 g of CH_3I in 250 ml of absolute ether) with cooling and stirring. After completion of the violent reaction, the mixture was stirred at room temperature for 1 hour, and was then decomposed with 170 g of ice and 20 ml of concentrated H_2SO_4. The resulting oxide was distilled with steam and 200 ml of distillate collected. The distillate was saturated with sodium chloride, the light upper layer which rose to the top separated, and the aqueous solution extracted 3 times with ether. The ether extracts were combined with the main oxide and dried over calcium chloride. After distilling off the ether, followed by two distillations of the residue over sodium, there resulted 13.5 g of 2,2-dimethylfuranidine (54% of theory); b.p. 92.2-92.4° (758 mm); n_D^{20} 1.4045; d_4^{20} 0.8441; MR_D 29.05. $C_6H_{12}O$. Calculated: MR_D 29.35.

Literature data: N. D. Zelinsky [3], b.p. 92-93° (746 mm); n_D^{21} 1.4063; d_4^{21} 0.8350; N. M. Kizhner and V. Klavikordov [4], b.p. 92.5-92.7° (764 mm); n_D^{20} 1.4075; d_0^{20} 0.8394.

Conversion of 2,2-dimethylfuranidine to 2,2-dimethylthiophane. 45 g of 2,2-dimethylfuranidine was passed over aluminum oxide at 350° at a rate of 0.6 ml/min. in a stream of hydrogen sulfide. The catalyzate was saturated with sodium hydroxide, the oily layer separated and dried over sodium hydroxide, followed by distillation. Upon distillation, the following fractions separated: 1st with b.p. 35-55°, 1.1 g; 2nd with b.p. 55-70°, 3.2 g; 3rd with b.p. 70-135°, 2 g; 4th with b.p. 135-142°, 16.2 g; 5th with b.p. 142-200°, 5.2 g; and a residue of 7.3 g, a viscous, semi-transparent mass. Fractions 1, 2 and 3 contained unsaturated compounds, but did not contain sulfur compounds. From the 4th fraction, after two distillations, 14.2 g of 2,2-dimethylthiophane (27% of theory) resulted: b.p. 138-138.8° (750 mm); n_D^{20} 1.4807; d_4^{20} 0.9220; MR_D 35.85. $C_6H_{12}S$. Calculated 35.68. The melting point of the compound with $HgCl_2$ was 131-133°. The 2,2-dimethylthiophane has not been described in the literature.

8.270 mg sub.: 18.800 mg CO_2; 7.480 mg H_2O; 6.730 mg SO_4. 7.750 mg sub.: 17.630 mg CO_2; 7.050 mg H_2O; 6.440 mg SO_4. Found %: C 62.03, 62.08; H 10.12, 10.18; S 27.81, 27.75. $C_6H_{12}S$. Calculated %: C 62.00; H 10.41; S 27.59.

Catalytic dehydration of 2,2-dimethylfuranidine. 75 g of 2,2-dimethylfuranidine was passed over aluminum oxide at 350° at a rate of 0.5 ml/min. in a stream of nitrogen. The receiver and the trap into which the catalyzate went, were cooled with an ice-salt mixture. The total weight of catalyzate was 60 g, the weight of the hydrocarbon layer was 46 g. After drying with calcium chloride, the hydrocarbon mixture was distilled (at 756 mm) on a column with an efficiency of 25 theoretical plates.

The following fractions were isolated: 1st, b.p. to 53°, 0.5 g, n_D^{20} 1.3842; 2nd, b.p. 53-57°, 2.0 g, n_D^{20} 1.3850, d_4^{20} 0.6677; 3rd, b.p. 57-60°, 1.0 g, n_D^{20} 1.3915; 4th, b.p. 66-69°, 2.0 g, n_D^{20} 1.4103, d_4^{20} 0.6846; 5th, b.p. 69-72°, 2.0 g, n_D^{20} 1.4207; 6th, b.p. 72-74.5°, 0.4 g, n_D^{20} 1.4360; 7th, b.p. 74.5°, 5.3 g, n_D^{20} 1.4470, d_4^{20} 0.7240; 8th, b.p. 75.4°, 3.0 g, n_D^{20} 1.4495, d_4^{20} 0.7186.

The residue, after cooling, polymerized to a colorless, vitreous mass.

The 2nd fraction, from its constants, corresponded to 2-methylpentene-3 (literature data: A. Gorsky [5], b.p. 57-58.5° at 760 mm; n_D^{20} 1.3883; d_4^{20} 0.6707); the 4th fraction resembled closely, in its boiling range, 2-methylpentene-2, but possessed a higher refractive index, apparently due to the presence of 2-methylpentadiene impurities (literature data of 2-methylpentene-2: C. Schmitt and C. Boord [6], b.p. 67.2-67.5° at 760 mm; n_D^{20} 1.4005; d_4^{20} 0.6904). The 7th and 8th fractions, judging from their constants, contained 2-methylpentadiene-1,3 (literature data [7]: b.p. 76° at 760 mm; n_D^{20} 1.4466; d_4^{20} 0.71896) and 2-methylpentadiene-2,4 (literature data: N. M. Kizhner and V. Klavikordov [4], b.p. 76-77.5°, n_D^{20} 1.4491; d_4^{20} 0.7229; N. Keersbilck [7], b.p. 76-76.5° at 759 mm; n_D^{20} 1.4532; d_4^{20} 0.7181). For more accurate evaluation of the contents of fractions 2, 3, 4, 7 and 8, they were investigated by the light dispersion method. The method of investigation, the apparatus and the materials used in this work were analogous to those described earlier [8]. For spectrum photography, the 2nd, 3rd and 4th fractions were combined. The combined dispersion spectrum (frequency range ω 200-1700 cm^{-1}) for the fractions investigated are given in the Tables, and spectra for the 7th and 8th fractions are shown parenthetically by darkening of the lines as determined by microphotographs, whereas for the spectrum of the 2nd, 3rd and 4th fractions, darkening is evaluated visually. The symbols used are: w = wide line (for the band), d = diffuse line, db = double line.

Spectrum for the Mixture of 2nd, 3rd and 4th fractions (b.p. 53-69°):

ω: **314** (0); **357** (2); **402** (1) d; 447 (1) w; 487 (0); **514** (2) db; 533 (3); **746** (1) w; **813-836** (5) w. db; **886-904** (2) w; 938 (1); 956-967 (1) db; **1014** (5); **1062** (2); 1104 (4); 1149 (2); 1170 (1); 1196 (1); **1217** (2); 1250 (1) d; **1304** (13); 1332 (2); **1359** (1) d; **1382** (10); 1414 (2); 1451 (10) w; 1601 (0); 1612 (4); 1641 (13); **1658** (15); 1678 (13).

The data given makes it possible, by measuring the most intense lines (bold type) [9], to determine quite reliably the presence of 2-methylpentene-2 in a mixture of the 2nd, 3rd and 4th fractions. From a series of lines, chiefly by the characteristic line 1672 cm^{-1} [9], can also be determined the presence of the trans isomer of 2-methylpentene-3. There should be taken into account literature data [9], according to which the spectrum for pure 2-methylpentene-3 was obtained on an apparatus with photoelectric recording with a wide slit ($\sim$11 cm^{-1}), because of which considerable deviation in frequencies (from 2 to 10 cm^{-1}) is possible.

Spectrum for the 7th Fraction (b.p. 74.5°):

ω: 200 (2) w; 246 (0) w; 306 (0); 363 (7); 436 (4); 447 (7); 476 (1); 495 (1); 526 (2); 535 (12); 587 (0) d; 680 (0) d; 706 (0) d; 770 (0) d; 812 (10); 827 (7); 860 (0), 882 (10) w; 897 (9) w; 935 (3); 960 (2); 992 (1); 1015 (20); 1041 (2); 1070 (2) d; 1103 (8), 1147 (15); 1157 (0) d; 1217 (24); 1246 (1) d; 1270 (8); 1293 (8); 1306 (32); 1332 (21); 1359 (2); 1380 (20); 1414 (14); 1453 (24) w; 1602 (29); 1612 (29); 1640 (20); 1660 (51).

Spectrum for the 8th Fraction (b.p. 75.4°):

ω: 200 (3) w: 362 (8); 437 (6); 447 (6); 480 (1); 495 (1); 524 (3); 535(9); 587 (0)d; 680 (0) d; 702 (0) d; 770 (0) d; 811 (9); 828 (3); 862 (1); 886 (2) d; 897 (10) sh; 935 (0); 964 (0); 1015 (16); 1040 (5); 1)68 (5); 1)89 (3) d; 11)3 (6); 1117 (3) d; 1148 (19); 1160 (5); 1217 (27); 1244 (1); 1268 (5); 1293 (15); 1306 (24); 1332 (24); 1354 (2); 1382 (19); 1415 (12); 1453 (23) w; 1603 (27); 1612 (15); 1640-1658 (47) w.

Darkening of weak lines was visually estimated by comparison with parallel standing lines measured by microphotogram.

The 7th and 8th fractions were mixtures of isomeric diene hydrocarbons with a conjugated double bond system, 2-methylpentadiene-2,4 and 2-methylpentadiene-1,3. Determination of the percent composition of each of these fractions was carried out by internal calibration method. In the fraction spectra, the relationships of intensities of the 1219 and the 1330 cm^{-1} lines to the intensity of the 669 cm^{-1} lines of chloroform added in specified amount, were measured photometrically, and on the basis of data on the line intensity for the spectrum of pure 2-methylpentadiene-2,4 [9], calculation of this hydrocarbon was carried out. It was found that the 7th fraction contained about 65% 2-methylpentadiene-2,4 and the 8th fraction about 80%; the content of 2-methylpentadiene-1,3 was determined by difference, i.e., it constituted 35% of the 7th fraction, and 20% of the 8th fraction. Proof of the presence of methylpentadiene-1,3 in the 7th fraction was also the resulting 2,4-dimethyl-Δ^3-tetrahydrophthalic acid. The 7th fraction in dioxane solution was treated with maleic anhydride in the presence of a small amount of hydroquinone. [10]. After hydrolysis and steam distillation, 2,4-dimethyl-Δ^3-tetrahydrophthalic acid separated, with m.p. 152°. Literature data: G. Bachman and G. Goebel [10]; m.p. 153-154°; R. Ya. Levina and co-workers [11]: m.p. 153°.

6.690 mg sub.: 13.713 mg CO_2; 4.450 mg H_2O. 5.860 mg sub.: 12.001 mg CO_2; 3.800 mg H_2O. Found %: C 55.94, 55.89; H 7.44, 7.26. $C_{10}H_{13}O_4 \cdot H_2O$. Calculated %: C 55.54; H 7.47.

SUMMARY

1. 2,2-Dimethylfuranidine, when passed over aluminum oxide in a stream of hydrogen sulfide at 350°, converts into 2,2-dimethylthiophane, and at the same time unsaturated hydrocarbons are produced.

2. Upon dehydrating 2,2-dimethylfuranidine over aluminum oxide at 350°, there is formed a mixture of hydrocarbons containing diene hydrocarbons with a conjugated double bond system: 2-methylpentadiene-2,4 and 2-methylpentadiene-1,3, as well as the ethylenic hydrocarbons: 2-methylpentene-2 and 2-methylpentene-3. Ethylenic hydrocarbons are found to be products of secondary reaction: the reduction of diene hydrocarbons with hydrogen resulting from destructive processes.

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ELECTROLYTIC DISSOCIATION IN ANHYDROUS SYSTEMS

I. STANNIC CHLORIDE-ETHYL ACETATE

S. P. Miskidzhyan

Numerous complex compounds found by physico-chemical methods of analysis in various bi-component systems have been defined in the general form, $nA \cdot mB$, owing to a lack of data regarding their structures. As examples, such known complex compounds as $C_3H_5CNS \cdot C_5H_{10}NH$; $C_6H_5NH_2 \cdot 2CH_3COOH$ and many other molecular compounds discovered by Academician N. S. Kurnakov and his students, can be cited.

Of special interest are those instances of complex formation wherein the components from which the complex compound is formed are non-electrolytes, while the complex compound resulting from them is a good conductor of the electric current. The above-mentioned compounds can be referred to as examples. Thus, the specific electroconductivity isotherm for the aniline-acetic acid system, studied for the first time by D. P. Konovalov [1], possesses a sharply-pronounced maximum, corresponding to the composition of the compound formed in the system. In like manner, corrected electroconductivity diagrams for such systems as allyl mustard oil-piperidine, and others, can be mentioned, from which it can be determined that the complex compound forming in the system is an electrolyte.

A clarification of the type of electroconductivity of similar complex compounds is of interest since it permits a clarification not only of the mechanism of electrolytic dissociation for these compounds, but also because it permits determination, to some degree, of the structures of these complexes, since, up to the present time, there can be found no data on the structures for a majority of the compounds in question.

A study of the electrolytic dissociation in anhydrous systems is also of considerable practical value for a clarification of the mechanisms of electrochemical processes for the industrial synthesis of a variety of products by electrolysis in organic solvents.

The author has selected stannic chloride-ethyl acetate, the viscosity of which and the electroconductivity of which have been studied by N. S. Kurnakov and E. B. Shternina [2]. According to these investigations, the system forms a complex compound of the composition $SnCl_4 \cdot 2CH_3COOC_2H_5$. Formation of such a compound is indicated by a sharply-defined maximum on the viscosity isotherms, the heats of combination, and the minimum on the electroconductivity diagram for this system [3, 4]. If one neglects the viscosity effect, then there will result on the electroconductivity diagram a maximum at approximately the composition of the compound, i.e., at 33.3 mole % stannic chloride, indicated by a high electroconductivity for the chemical compound formed in the system. As is known, none of the components of this system will conduct the electric current. Thus, for example, the specific electroconductivity for ethyl acetate and stannic chloride is $\kappa < 10^{-9} \Omega^{-1} cm^{-1}$. It seemed to the author, therefore, that a study of the electrolytic dissociation mechanism and the nature of the conductivity of the compound could lead to a determination of a structure for the complex.

EXPERIMENTAL

To study the nature of conductivity of the electric current, electrolysis of the above-indicated complex compound was carried out with various mixtures of this system, followed by investigation of the composition and some of the physical properties of the liquid areas around the anode and the cathode, before and after electrolysis.

Electrolysis was carried out in an H-shaped vessel with platinum electrodes, where the cathode space was separated from the anode. A lamp rectifier with terminal voltage of 300 V served for the current source. To measure the amount of electricity, a copper coulometer was switched into the circuit. The current strength fluctuated from 2 to 5 mA at the start of the experiment, and from 15 to 20 mA at the end. Duration of experiments lasted from 8 to 48 hours. Temperature varied from 16 to 19°.

Chemical analysis of the composition of the mixture and of liquid in the anodic and cathodic areas after the electrolysis was carried out as follows. The quantity of tetravalent tin was determined by precipitating it in the form of hydroxide, and subsequent calcining to SnO_2 [5]. The quantity of ethyl acetate in the run was calculated by weight difference in tin tetrachloride for the run. A preliminary control determination indicated that the presence of ethyl

acetate does not interfere with tin determination. Tin tetrachloride was obtained by passing chlorine through chemically-pure tin foil [6]. The resulting tin tetrachloride was distilled. The fraction boiling at 112-114° was taken for the work. Density of the preparation obtained at 0° was 2.276. To prepare the second component, the author used ready-prepared, chemically-pure ethyl acetate, which had been kept over anhydrous sodium acetate and sodium carbonate for several days, and distilled with precautionary measure against access of moisture. The fraction boiling at 76-77.5° was collected. Density of the distilled ethyl acetate was 0.9002 at 20°, and the refractive index at the same temperature was 1.3722.

Two initial mixtures were prepared for the investigation: first, from 20 mole % tin tetrachloride and 80 mole % ethyl acetate, and the second mixture of 60 mole % tin tetrachloride and 40 mole % ethyl acetate. A mixture of such composition was taken because such ratios of components corresponded to the maximum electroconductivity for this system.

Preparation of these mixtures was carried out in an H-shaped vessel, as was done by N. S. Kurnakov [3]. In such a vessel gradual mixing of the components, and of cooling, is assured, since otherwise the mixture evolves heat spontaneously due to the heat of chemical reaction, and leads to a partial resinification.

Electrolytic data are given in Table 1 for various mixtures of the system studied by the author, along with the analytical results of liquids at the anodic and cathodic areas, after electrolysis.

TABLE 1

Expt. No.	$SnCl_4$ content in the mixture before electrolysis (in weight %)	$SnCl_4$ content after electrolysis (in %)				Amount of electrolyte passed through the solution (in coulombs)
		in liquid of the anode space	change	in liquid of the cathode space	change	
1	46.91	50.11	+3.60	–	–	318
2	39.10	50.56	+11.46	27.13	−11.97	753
3	39.10	44.76	+5.66	28.41	−10.79	676
4	44.23	48.41	+4.18	38.26	− 5.97	520
5	80.77	84.50	+3.73	80.31	− 0.46	250

There is given in the second column of the Table the composition of the initial mixtures found on the basis of chemical analysis.

The following phenomena were observed during electrolysis:

1) directly following switch-on of the current, accumulation of a gray precipitate of metallic tin occurred at the cathode;

2) at the completion of electrolysis, current increased markedly, due to heating of the liquid at the expense of Joules of heat at the cathode, at which a white precipitate separated, which, by chemical analysis, proved to be $SnCl_2$;

3) evolution of gas bubbles was not observed at the anode; some evolution of gas bubbles was observed at the cathode at the end of an experiment in some cases (when electrolysis had been continued for a long time).

On the basis of Table 1 data, and observations during electrolysis, the following assumptions can be made with regard to the mechanism of electrolytic dissociation of the complex compound in the system, and with regard to the electrochemical processes occurring at the anode and cathode during electrolysis.

1. Apparently, molecules of the complex compound in the system are associated, and are in the form of $(SnCl_4 \cdot 2CH_3COOC_2H_5)_n$. This is indicated by the presence of a sharp maximum on the viscosity isotherm for this system, which occurs at a composition of 1:2, i.e., at the composition of the complex compound forming in the system. On the other hand, the viscosity of the complex compound exceeds by about 250-fold the viscosity of the most viscous of the components, which, in all probability, is related to an association phenomenon for the complex compound molecules. A. N. Sakhanov [7] pointed out formation of associated complex compounds in current-conducting systems.

2. If the presence of association of complex compound molecules is assumed to be possible for the system, then the main process of electrolytic dissociation can be represented in the following manner:

$$SnCl_4 \cdot 2CH_3COOC_2H_5)_2 \rightleftharpoons [Sn(CH_3COOC_2H_5)_4Cl_2]^{++} + [SnCl_6]^{--}$$

In this case we take the position that aggregated molecules with a high number, n, break down into smaller aggregates, where n = 2.

Along with this main process, there apparently proceeds, although on a small scale, a further electrolytic dissociation of the cation according to the following scheme:

$$[Sn(CH_3COOC_2H_5)_4Cl_2]^{++} + SnCl_4 \rightleftharpoons [Sn(CH_3COOC_2H_5)_4]^{++++} + [SnCl_6]^{--}]$$

3. With electrolysis at the electrodes, the following electrochemical processes apparently take place.

At the cathode. At the start of electrolysis, when the ions obtained at the expense of the second dissociation stage are sufficient in number, metallic tin separates at the cathode according to the following reaction:

$$[Sn(CH_3COOC_2H_5)_4]^{++++} + 4e \rightarrow Sn + 4CH_3COOC_2H_5.$$

At high current densities, when there is a shortage of tin ions due to the small rate of electrolytic dissociation of the second stage, $SnCl_2$ separates at the cathode according to the following reaction:

$$[Sn(CH_3COOC_2H_5)_4Cl_2]^{++} + 2e \rightarrow 4CH_3COOC_2H_5 + SnCl_2.$$

The following facts serve to confirm the indicated processes:

a) Separation of metallic tin at the cathode.

b) Separation of $SnCl_2$ as a white precipitate at the cathode; the phenomenon of simultaneous separation of the metal and the salt of the metal at the cathode is known in the literature. Thus, for example, Watkins and Denham [8] indicated the fact that upon electrolysis of aqueous or alcoholic solutions of cupric chloride or bromide, the precipitates were composed of a heterogeneous mixture of copper with copper halide, where the quantity of halide was greater in proportion as the current density was greater. Gore [9], electrolyzing a hydrochloride solution of antimony trichloride, found up to 5% $SbCl_3$ in the metallic precipitate of antimony.

c) The increase in percentage composition of ethyl acetate in the liquid of the cathode space after electrolysis, occurs because of a break-down of the complex ions

$$[Sn(CH_3COOC_2H_5)_4]^{++++} \text{ and } [Sn(CH_3COOC_2H_5)_4Cl_2]^{++}$$

during their discharge at the cathode.

At the anode. The anion discharge apparently proceeds as follows:

$$[SnCl_6]^{--} \rightarrow SnCl_4 + 2Cl + 2e.$$

Atomic chlorine at the moment of evolution enters into reaction with a molecule of ethyl acetate and chlorinates the methyl group:

$$CH_3COOC_2H_5 + 2Cl \rightarrow CH_2ClCOOC_2H_5 + HCl.$$

This assumption appears more probable if there be taken into consideration the literature data [10] with the fact that $SnCl_4$ is found to be a catalyst for chlorination of certain organic compounds. The hydrogen chloride evolved during chlorination interacts with $SnCl_4$ forming

$$2HCl + SnCl_4 \rightleftharpoons H_2SnCl_6.$$

This compound, and perhaps HCl also, has apparently accumulated by the end of the experiment in adequate amount for self-electrolysis to take place according to the reaction:

$$H_2SnCl_6 \rightleftharpoons 2H^+ + SnCl_6^{--}$$

or

$$HCl \rightleftharpoons H^+ + Cl^-,$$

by which time the evolution of gas bubbles at the cathode is limited.

As proof of the fact that the above-indicated reaction occurs at the anode, can be cited the following data: a) a noticeable increase in the stannic chloride content for the liquid of the anode space after electrolysis (Table 1); no evolution of gaseous chlorine at the anode, due to reaction with ethyl acetate molecules, as confirmed by the presence in the ether extract of an organic compound having in its composition chloride ion extracted from the aqueous solution of the anodic space liquid (after electrolysis). Chlorine was found by both the Beilstein method, and by reacting the organic substance with metallic sodium, and subsequent identification of chloride ion by use of silver nitrate.

In order to remove doubt that the chlorine could have gotten into the extracted substance from the aqueous medium where $SnCl_4$ and HCl are present in sufficient amounts, an analogous extraction from initial liquid was carried out, i.e., from the mixture before electrolysis; in this case both tests for chloride were negative.

Another proof of HCl formation in the anode space is given by the fact that the chloride ion precipitated with silver nitrate from the anode area liquid (after electrolysis) using the theoretical quantity of silver nitrate dissolved in water, the required amount of silver nitrate is noticeably greater than that required by calculating on the basis of tin tetrachloride content in the mixture. If the quantity of electricity passed through the solution is accounted for, and the amount of HCl taken into account, which could have been formed in this manner, the correspondence is then approximately in accord with the excess silver nitrate used to precipitate the chloride ions.

Electrolysis of the second of the initial mixtures proceeds, on the whole, as with electrolysis of the first mixture. The difference consists in the fact that in this case a gray precipitate separates (metallic tin) to a considerably greater extent than in the first case. This is explained by the fact that with an excess of tin tetrachloride molecules, the second stage of electrolytic dissociation:

$$[Sn(CH_3COOC_2H_5)_4Cl_2]^{++} + SnCl_4 \rightleftharpoons [Sn(CH_3COOC_2H_5)_4]^{++++} + [SnCl_6]^{--}$$

proceeds with considerably greater slowness.

Some additional proofs of the above-given electrochemical processes proceeding at the anode and cathode during electrolysis of mixtures of the system studied by the author were obtained when a number of physico-chemical constants for the initial mixture and for the anode and cathode area liquids after electrolysis were determined.

In Table 2 there are given the density and apparent molecular weights for the liquids of the anode and cathode area before and after electrolysis.

It can be seen from data given in this table that the density for the mixture in the anode area after electrolysis increases, and decreases in the cathode area. This is in agreement with a clarification of the electrode processes given above. An increase in density of the anode area liquid is caused by the increase in percent content of tin chloride after electrolysis, the density of which is approximately 2-fold greater than the density of the initial mixture.

TABLE 2

Content of $SnCl_4$ in the mixture (weight %)	Density d^{25}			Apparent molecular weight, M			Amount of electricity passed (in coulombs)
	before electrolysis	after electrolysis		before electrolysis	after electrolysis		
		anode area	cathode area		anode area	cathode area	
44.23	1.3470	1.4654	1.2526	281.5	511.4	224.5	520
80.77	1.8570	1.8789	1.8121	334.8	479.4	332.5	250

Decrease in density of the cathode area liquid is related to the increase in percent content of ethyl acetate after electrolysis as a result of the discharge of complex cations. With regard to the apparent molecular weight (measured cryoscopically in benzene solvent), here again, the sharp increase in apparent molecular weight of anode area liquid after electrolysis is explainable by the fact that the $SnCl_6^{--}$ ions, being discharged at the anode, form an additional amount of tin tetrachloride. The latter, by entering into combination with ethyl acetate which is present in excess (in the case of the 20 mole % stannic chloride mixture) forms new molecules of the complex compound: $(SnCl_4 \cdot 2CH_3COOC_2H_5)_n$, the molecular weight of which is much greater than that of the initial mixture.

A noticeable decrease in apparent molecular weight for the cathode area liquid after electrolysis is explainable on the basis that upon destruction of the complex cations $[Sn(CH_3COOC_2H_5)_4]^{++++}$ and $[Sn(CH_3COOC_2H_5)_4Cl_2]^{++}$, the amount of ethyl acetate increases, the molecular weight of which is relatively small.

SUMMARY

1. Electrolysis of a mixture of stannic chloride and ethyl acetate has been carried out.

2. On the basis of data obtained by chemical analysis of liquids at the anode and cathode area, before and after electrolysis, and on the basis of measurements of a series of physico-chemical properties for these liquids, a conclusion has been made concerning the mechanism of dissociation of the complex compound.

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KINETICS OF THE CHLOROSULFONATION REACTION. II.

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There have appeared during the past few years a number of works [1, 2, 3, 4] in which kinetics of the chlorosulfonation process has been discussed to some extent; from the present author's point of view, these authors have proceeded from inaccurate premises regarding the reaction mechanism, because of which they came to erroneous conclusions.

Based upon a specifically-defined concept concerning the mechanism of the chlorosulfonation process earlier discussed [5], the author has analyzed the equation for individual reaction rates and has determined experimentally the kinetic curves for accumulation of sulfonyl chlorides during the reaction of chlorosulfonic acid with acetanilide and carbanilide (diphenylurea).

Consider reaction of an aromatic compound, ArH, with chlorosulfonic acid. For the sake of simplification, let it be assumed that this compound does not possess substituents which can interact with chlorosulfonic acid (for example, benzene), so that interaction leads only to formation of monosulfonic acid and monosulfonyl chloride. Thus, formation of polysulfonic acid derivatives, isomeric compounds, sulfones, and others, which in reality do occur to some extent upon chlorosulfonation of various compounds, is excluded by the author from playing any important role. Equally well excluded is the probability of sulfonic acid formation from the ArH compound and sulfuric acid, inasmuch as it was demonstrated earlier by the author [1] that this process proceeds much slower and does not play an important role in chlorosulfonation.

On the basis of the above, the processes can be represented by four major schemes [5].

$$ArH + ClSO_3H \rightarrow ArSO_3H + HCl, \quad (1)$$

$$ArH + 2ClSO_3H \rightarrow ArSO_2Cl + HCl + H_2SO_4, \quad (2)$$

$$ArSO_3H + ClSO_3H \rightarrow ArSO_2Cl + H_2SO_4, \quad (3)$$

$$ArSO_3H + ClS_3OH \leftarrow ArSO_2Cl + H_2SO_4 \rightarrow ArSO_3H + SO_3 + HCl \quad (4)$$

We might designate the following for molar concentrations of reacting substances: of an aromatic compound, A; of chlorosulfonic acid, B; of sulfuric acid, C; the degree of sulfonation (or chlorosulfonation) of the ArH compound, by the variable X, at a given moment of time; and the ratio of molar concentration of sulfonic acid to the concentration of sulfonated products at the moment, t, by the variable Y. The concentration of sulfonic acid will then be expressed as XY, and concentration of sulfonyl chloride as X(1−Y).

If K_1, K_2, K_3 and K_4 are taken as the rate coefficients for the corresponding reactions, then the rate equations for these reactions can be represented as follows (accepting that $K_4 = K_4(\leftarrow) + K_4(\rightarrow)$:

$$\frac{dx_1}{dt} = K_1 \cdot (A-X) \cdot (B-X), \quad (5)$$

$$\frac{dx_2}{dt} = K_2 \cdot (A-X) \cdot (B-2X), \quad (6)$$

$$\frac{dx_3}{dt} = K_3 \cdot XY \cdot [B-X(2-Y)], \quad (7)$$

$$\frac{dx_4}{dt} = K_4 \cdot X(1-Y) \cdot [C + X(1-Y)]. \quad (8)$$

The summated rates for formation of sulfonic acid and sulfonyl chloride will be expressed by the equations:

$$\frac{dx_5}{dt} = K_1(A-X)(B-X) - K_3XY[B-X(2-Y)] + K_4X(1-Y)[C + X(1-Y)],$$

$$\frac{dx_6}{dt} = K_2(A-X)(B-2X) + K_3XY[B-X(2-Y)] - K_4X(1-Y)[C + X(1-Y)].$$

At the moment when X becomes equal to A, i.e., all of the ArH substance has reacted, having become converted to the sulfonic acid, with concentrations AY, and to sulfonyl chloride with $A(1-Y)$ concentration, reactions (1) and (2) cease because

$$\frac{dx_1}{dt} = 0 \text{ and } \frac{dx_2}{dt} = 0.$$

But reactions (3) and (4) will continue, which is the reason why excess chlorosulfonic acid was taken, i.e., if $B > 2A$, then the rate of formation of sulfonic acid and of sulfonyl chloride will be expressed by the equation:

$$\frac{dx_5}{dt} = -K_3AY[B-A(2-Y)] + K_4A(1-Y)\cdot[C + A(1-Y)],$$

$$\frac{dx_6}{dt} = K_3AY[B-A(2-Y)] - K_4A(1-Y)[C + A(1-Y)],$$

i.e., the latest process occurs in such manner as though it were reversible.

Let us assume that the system is in a state of equilibrium, as some investigators have accepted [2, 3].

If such is the case, then in the equilibrium state, the combined rate of formation of sulfonic acid and sulfonyl chloride will be equal to zero, i.e.,

$$\frac{dx_5}{dt} = 0 \text{ and } \frac{dx_6}{dt} = 0, \text{ hence:}$$

$$K_3AY_E[B-A(2-Y)] = K_4A(1-Y_E)[C + A(1-Y_E)]$$

or

$$\frac{Y_E}{1-Y_E} = \frac{K_4}{K_3}\cdot\frac{C + A(1-Y_E)}{[B-A(2-Y_E)]} = K_E\cdot\frac{C_E}{B_E}. \quad \ldots \quad (9)$$

Thus, the ratio of sulfonic acid and sulfonyl chloride yields in the state of presumed equilibrium should be determined by the ratio of the reaction rate constants (4) and (3), and by the ratio of sulfuric acid concentration in the equilibrium state, C_E, to the concentration of chlorosulfonic acid, B_E.

Let us examine upon what the ratio of sulfuric acid to chlorosulfonic acid in that state depends:

$$\frac{C + A(1-Y_E)}{B-A(2-Y_E)} = \frac{\frac{C}{A} + (1-Y_E)}{\frac{B}{A} - (2-Y_E)}$$

Hence it can be seen that the yields of sulfonic acids and of sulfonyl chlorides in the state of presumed equilibrium, along with other factors, are determined (primarily) by the ratio of initial concentration of sulfuric acid to that of sulfonating agent $\frac{C}{A}$, and by the ratio of initial concentration of chlorosulfonic acid to sulfonating agent $\frac{B}{A}$.

Let us find the derivative for the function $\frac{dx_4}{dt}$, equating it to zero, and using the specifically determined value, Y, from the resulting equation which corresponds to the extreme value for the function, and let us substitute it into the function. We thereby get interesting results which have significant practical value, namely:

$$\left(\frac{dX_4}{dt}\right)_{extr} = -K_4\cdot\frac{C^2}{4}.$$

Hence it can be seen that the extreme value for the decomposition rate of sulfuric acid and sulfonyl chloride (a process undesirable from the standpoint of practical production of chlorosulfonate) is a value which depends upon the initial concentration of sulfuric acid at the second stage.

These conclusions refute the claim of L. S. Solodar and Z. I. Shevchenko [1] that sulfuric acid does not play any role in the chlor sulfonation and that this is in complete agreement with their experimental data, with those of Spryskov [2, 3], and with those of the present author.

In using Equation (9), the author assumed that the system is in equilibrium. We might examine the accuracy of this assumption.

Take sulfonic acid, chlorosulfonic acid and sulfuric acid in the initial stage, where their concentrations are respectively equal to S, B, and C. Assume during the time, t, that X moles of sulfonic acid are converted to the sulfonyl chloride. In this case there is formed X moles of sulfonyl chloride and X moles of sulfuric acid, which interact further according to Reactions (3) and (4).

It should be taken into account in this case that the reaction between sulfonyl chloride and sulfuric acid actually proceeds in part with evolution of sulfur trioxide and hydrogen chloride, and not with evolution of chlorosulfonic acid, as was assumed by Spryskov [2, 3].

In fact, if one proceeds from sulfonyl chloride and pure sulfuric acid, rather than from a mixture of sulfuric acid and chlorosulfonic acid, then the reaction will proceed until such time when all of the sulfonyl chloride has converted to the sulfonic acid, and no equilibrium between sulfonyl chloride and sulfonic acid can be observed.

Equations of rate for Reactions (3) and (4) in the units adopted can be presented as follows:

$$\frac{dx_3}{dt} = K_1 (S-X) \cdot (B-X),$$

$$\frac{dx_4}{dt} = K_2 \cdot X (C + X), \text{ where } K_2 = K_2(\leftarrow) + K_2(\rightarrow).$$

The equation for the overall process rate will be:

$$\frac{dx}{dt} = K_1(S-X) \cdot (B-X) - K_2 X (C + X). \tag{10}$$

To simplify the conclusions, let us take C = 0 and S = B = 1, whereupon Equation (10) will be expressed:

$$\frac{dX}{dt} = K_1 (1-X)^2 - K_2 X^2. \tag{11}$$

As X increases, the first member of the equation decreases, and consequently the second will increase, and at a determined value for X, the rate sum of the process can become equal to zero, which will define a "pseudoequilibrium" state for the system. In fact, modified curves of the $\frac{dx}{dt}$ function in relation to X, as represented in Fig. 1, pass through zero with a free selection of K_1 and K_2 values (taken within the range observed for the experiment). However, this state is not found to be truly an equilibrium, but rather a "pseudoequilibrium", inasmuch as further course of Reactions (3) and (4) takes the system out of this state, and the modified rate for sulfonyl chloride quantity (X) with time acquires a negative value, which indicates decrease in the amount of sulfonyl chloride after passage through a maximum.

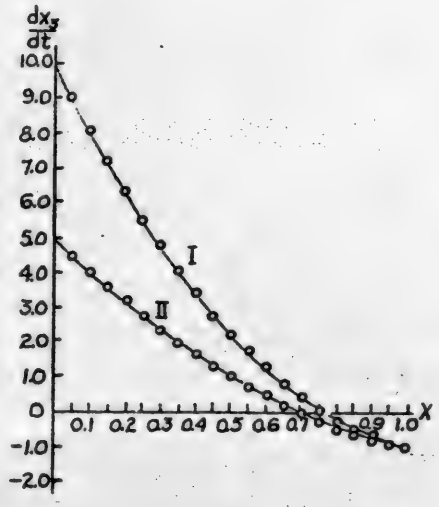

Fig. 1. Calculated curves for Function (11) Modification. I) For $K_1 = 10$ and $K_2 = 1$; II) for $K_1 = 5$ and $K_2 = 1$.

Inasmuch as in Reaction (3) the concentration of chlorosulfonic acid decreases continuously, while the concentration of sulfuric acid increases, nonetheless, a decrease in sulfuric acid concentration during the course of Reaction (4) does not lead to a corresponding increase in concentration of chlorosulfonic acid, and the hydrogen chloride which is evolved leaves the zone of interaction, in which case the actual equilibrium state will, of course, be the state of the process, i.e., at that state where there will be present in the reaction mixture the following concentrations: chlorosulfonic acid, 0; sulfonyl chloride, 0; sulfonic acid, S, sulfuric acid, C + B.

Consequently, in the general case where $C \neq 0$ and $S \neq B \neq 1$ a pseudoequilibrium state is possible:

$$\frac{dx}{dt} = 0 \quad K_1 (S-X_{PE})(B-X_{PE}) = K_2 X_{PE} (C + X_{PE}),^*$$

hence

$$\frac{X_{PE}}{S-X_{PE}} = \frac{K_1}{K_2} \cdot \frac{B-X_{PE}}{C + X_{PE}} = K_{PE} \cdot \frac{B-X_{PE}}{C + X_{PE}} \tag{12}$$

i.e., the ratio of sulfonyl chloride to the amount of sulfonic acid in the pseudoequilibrium state depends upon the ratio of reaction rate

* Subscript PE = pseudoequilibrium.

constants and the ratio of chlorosulfonic acid concentration to the sulfuric acid concentration at the end of the process, and depends only upon those factors we have already mentioned.

To reach high yields of sulfonyl chloride in chlorosulfonation practice, a high concentration of chlorosulfonic acid should be maintained and a low concentration of sulfuric acid, the process should be interrupted at the pseudo-equilibrium state, and should be carried out at such temperature conditions as $K_1 \gg K_2$.

Solution of Equation (12) in relation to X_{PE} gives:

$$X_{PE} = \frac{K_{PE}(B + S) + C \pm \sqrt{[K_{PE}(B + S) + C]^2 - 4(K_{PE} - 1)K_{PE}BS}}{2(K_{PE} - 1)},$$

which is in agreement with the formula developed by Spryskov [2] with regard to the true equilibrium state. It actually however, should be regarded as a reflection of the sulfonyl chloride concentration in the "pseudoequilibrium" state.

To determine the form of the summated rate process curve, we can graphically present the individual reaction rates (1, 2, 3 and 4) according to the rate equations (5, 6, 7 and 8) for the process at random values A, B, C, K_1, K_2, K_3 and K_4 selected within the range found in chlorosulfonation practice (Fig. 2).

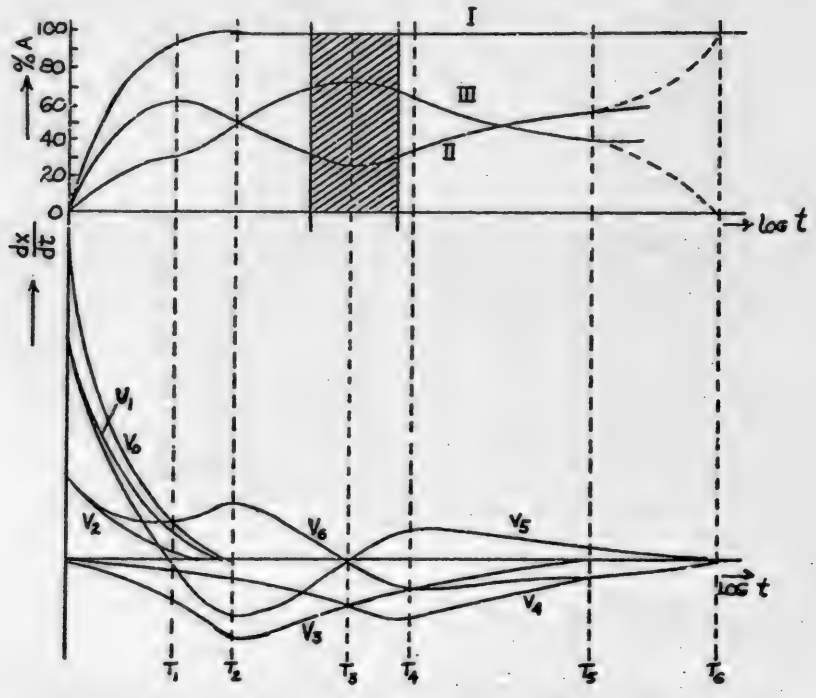

Fig. 2. Graphical presentation of a mathematical analysis of the principal reaction rate (1)-(4) equations which occur during chlorosulfonation of aromatic compounds.

We shall take into account here that: 1) a large excess of chlorosulfonic acid is used, i.e., $B > 2A$; 2) X = degree of sulfonation of the substance, which can be changed within the range X = 0 to X = A; 3) Y = relative content of sulfonic acid in the mixture of sulfonated compounds, and can be varied from Y = 0 to Y = 1; 4) for given changes in the variable X and Y, the $\frac{dx_1}{dt}$, $\frac{dx_2}{dt}$, $\frac{dx_3}{dt}$ and $\frac{dx_4}{dt}$ functions are continuous, as can be readily demonstrated.

Let us assume that: $K_1 > K_2$, $K_3 > K_4$ and $K_2 \gg K_3$, i.e., $K_1 > K_2 \gg K_3 > K_4$, which is in agreement with the experimental data.

The curves are plotted for the system $\frac{dx}{dt} - \log t$.

Functions (5), (6), (7) and (8) are represented by the curves v_1, v_2, v_3 and v_4, respectively, (lower curves in Fig. 2); v_1 and v_2 are plotted up from the abscissa axis, reflecting processes of accumulation in the reaction mixture of sulfonic

acid and sulfonyl chloride; curves $\underline{v}_3$ and $\underline{v}_4$ are tentatively plotted downward from the abscissa axis, inasmuch as they reflect the reactions involving loss of these same substances.

Let us reproduce a graphical construction of the modified curves for the rate of conversion of the sulfonated compound $\underline{v}_0 = \underline{v}_1 + \underline{v}_2$, which changes the rate of sulfonic acid formation with simultaneous run of all processes: $\underline{v}_5 = \underline{v}_1 - \underline{v}_3 + \underline{v}_4$ and of sulfonyl chloride $\underline{v}_6 = \underline{v}_2 + \underline{v}_3 - \underline{v}_4$.

By carrying out a graphical integration of the functions obtained, we can construct curves I, II, and III (upper curves of Fig. 2) which express the change with time: I = amount of compound sulfonated (by $\underline{v}_0$), II = amounts of sulfonic acids formed (by $\underline{v}_5$), III = amount of sulfonyl chloride formed (by $\underline{v}_6$).

Let us analyze the resulting curves.

Curve I increases rapidly up to point T_2, whereupon it reaches a maximum value equal to A (100%), and then proceeds parallel to the abscissa axis, inasmuch as $\underline{v}_0 = 0$.

Curve II has a maximum at point T_1, since $(\underline{v}_5)_{T_1} = 0$, and it then begins to decrease because the rate of sulfonic acid formation becomes negative. At point T_3, the curve is at a minimum $(\underline{v}_5)_{T_3} = 0$, and then increases to maximum value at point T_6.

Curve III increases all the time up to point T_3, where it possesses a maximum, inasmuch as $(\underline{v}_6)_{T_3} = 0$. Beyond that, the rate of formation of sulfonyl chloride ($\underline{v}_6$) becomes negative, in connection with which the curve gradually falls, reaching 0 at point T_6.

Thus, the graph for the summated process has along the time axis the four following characteristic points.

Point T_1, in which the formation rate for sulfonic acid is equal to zero at the same time that the formation rate for sulfonyl chloride is not equal to zero. The points correspond to the maximum quantity of sulfonic acid formed. In the experiments, this point was not attained when time, T_2, was too short, especially at elevated temperature.

Point T_3 is the second characteristic point at which $(\underline{v}_5)_{T_3} = 0$ and $(\underline{v}_6)_{T_3} = 0$. This point corresponds to the maximum amount of sulfonyl chloride formed for a minimum quantity of sulfonic acid. Point T_3 is the pseudo-equilibrium point, and is not a true equilibrium, inasmuch as beyond this point $\underline{v}_4 - \underline{v}_3 \neq 0$.

Point T_5 is the third characteristic point, because it corresponds to the zero rate for the following processes: $(\underline{v}_3)_{T_5} = 0$ while rates for the other processes are other than 0.

Point T_6 is the point of final state for the process because at this point the rates for all of the processes are equal to zero.

This point corresponds to that state where there is no chlorosulfonic acid in the system, and all of the sulfonyl chloride has been converted to the sulfonic acid. The system consists of only three components — sulfuric acid, sulfonic acid and sulfur trioxide.

It should be mentioned that in the period of time close to T_3 (shaded in the figure), the change in amount of sulfonyl chloride in the system occurs very slowly. Determination of the amount of sulfonyl chloride in the system for this period of time, after taking into account experimental and analytical errors, gives almost constant results. This situation leads to the conclusion that a number of investigators have taken this period to be the true equilibrium state (Solodar, Spryskov and others). Partially erroneous conclusions were drawn to the effect that chlorosulfonation should be carried out within a time period not less than that determined, and that longer time for the reaction course does not result in decreasing the yield of sulfonyl chloride [6]. As can be seen, such a viewpoint of the problem is harmful to the practice of chlorosulfonation. The process should be interrupted at a point as close as possible to the pseudoequilibrium point, T_3.

To verify conclusions drawn on the basis of an analysis of the kinetic equations, the author undertook to experimentally investigate change in the quantity of sulfonyl chloride over an interval of time, reacting the chlorosulfonic acid with diphenylurea at 25° and with acetanilide at 25° and 40°.

The diphenylurea was purified by two recrystallizations from absolute ether, and the acetanilide from alcohol. Technical chlorosulfonic acid was distilled in vacuo (78-80° at 21-25 mm) and contained 98.1% of $ClSO_3H$ according to chlorine analysis. The process was carried out in a thermostat and to maintain a specified temperature, solid carbon dioxide was introduced into the reaction mixture at the start of the reaction to remove heat of reaction. After determined intervals of time, the sulfonic mixture was aspirated into an ampoule, the latter sealed and broken under water in a closed vessel. Calculation of the sulfonyl chloride formed was carried out on the basis of determination of "inorganic" and "organic" chlorine, utilizing the Volhard method. The resulting data are given in Fig. 3.

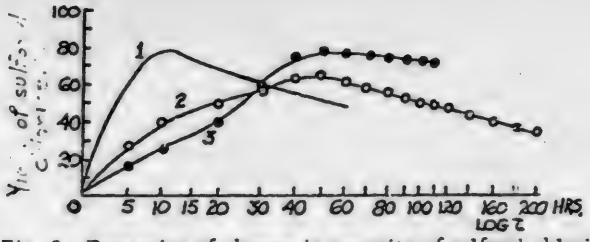

Fig. 3. Dynamics of change in quantity of sulfonyl chlorides in the reaction mixture during chlorosulfonation. 1) Acetanilide at 40°; 2) acetanilide at 25°; 3) diphenylurea at 25°.

A comparison of the curves constructed according to experimental data with the integral curves analytically constructed (Fig. 2) indicates sufficiently good coincidence in the nature of the curves.

Characteristic for these curves, aside from the extreme points, is the presence of deflection points, both for ascending and descending branches of the curves.

The presence of these points confirms the complex mechanism for the process and the coexistence of a number of reactions whose courses are varied. This confirms the accuracy of the reaction mechanism, determined by the author, which occurs upon chlorosulfonation of aromatic acyl amines [5], which is expressed by aggregate of Equations (1)-(4).

SUMMARY

1. A mathematical analysis of the rate equations for individual reactions which occur upon chlorosulfonation of aromatic acylamines has been carried out according to the mechanism determined earlier by the author [5]. The resulting integral curves of molar amounts of sulfonyl chloride changing with time in the reaction mixture agree well with the curves constructed from experimental data for chlorosulfonation of acetanilide and of diphenylurea.

2. It has been determined that the aromatic compound-chlorosulfonic acid system comes to a pseudoequilibrium state with time, which can be maintained unchanged for a prolonged length of time relative to the amounts of sulfonyl chloride and sulfonic acid, and this was earlier considered erroneously to have been the true equilibrium state.

3. It has been demonstrated that the maximum yield of sulfonyl chloride is reached at the pseudoequilibrium state, and is determined by the ratio between the reaction rates (3) and (4). Consequently, for a given compound and temperature, it is determined by the relation of chlorosulfonic acid and sulfuric acid concentrations to the concentration of chlorosulfonated compound.

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* See Consultants Bureau Translation, page 787.

** See Consultants Bureau Translation, page 2097.

*** See Consultants Bureau Translation, page 113.

POLAROGRAPHIC INVESTIGATION OF THE HYDROGENATION PROCESS

II. HYDROGENATION OF MALEIC AND FUMARIC ACID MIXTURES

A. L. Markman

The behavior of cis- and trans-ethylenes is an individual problem in catalytic hydrogenation of ethylene compounds. Paal and Schiedewitz [1], Ott [2], and Golendeev and Plisov [3], who hydrogenated, individually, various geometric isomers, have found that the saturation rate for cis-isomers is always higher than for trans-isomers.

The author has not found in the literature information on the behavior of cis- and trans-isomers when they are hydrogenated as combined mixtures; nor any general description on combined hydrogenation experiments. The author, therefore, undertook a study of the behavior of maleic and fumaric acids during their separate and their combined hydrogenation.

Maleic acid was prepared from chemically-pure maleic anhydride and purified by three recrystallizations from aqueous solution. After drying, the m.p. was 130°. The fumaric acid was chemically-pure when used.

The author carried out a number of experiments on separate hydrogenations of the acids named with platinum and with palladium catalysts which were precipitated onto aluminum and nickel supports, as the result of which the hydrogenation rate constants were determined, which are given in Table 1. The experimental procedure was the same as described earlier [4].

It can be seen from Table 1 data that the relationship of the saturation rate constants for maleic and fumaric acids to the nature of the catalyst, and its amount, varies over quite a wide range —from 0.92 to 9.29, and in the majority of cases, maleic acid saturates more rapidly than fumaric acid.

In the hydrogenation of maleic-fumaric acid mixtures, the author has developed a method for their combined polarography. The author has established that these acids give two different waves upon reduction at the dropping mercury cathode, in absolute ethyl alcohol acidified with 0.1 N hydrochloric acid, and which differ in the half-wave potential values by 0.2 V, the difference amounting to 0.17-0.18 V in 95-96% alcohol. This circumstance was utilized by the author to analyze mixtures of maleic and fumaric acids during the course of their hydrogenation.

TABLE 1

Expt. No.	Acid hydrogenated (0.005 mole)	Catalyst	Amount of catalyst (in mg)	Metal support	Amount of metal support (in mg)	Hydrogenation rate constants	Ratio of the constants, $k_{maleic}/k_{fumaric}$
157	Maleic	Pd	32	Ni	105	0.088	0.92
153	Fumaric					0.960	
45	Maleic	Pd	64	Ni	105	0.188	2.29
152	Fumaric					0.082	
103	Maleic	Pd	32	Al	105	0.0468	6.59
154	Fumaric					0.0071	
107	Maleic	Pd	64	Al	210	0.0613	9.29
155	Fumaric					0.0066	
19	Maleic	Pt	58	Ni	105	0.0190	2.00
16	Fumaric					0.0095	

The sequence of carrying out experiments on combined hydrogenation of the two geometrically isomeric acids is given.

1. Hydrogenation of Maleic-Fumaric Acid Mixture with Palladium Catalyst

Experiment 104. 0.58 g of maleic and 0.58 g of fumaric acids (in 1/200 mole portions), 210 mg of Al and 64 mg of Pd, 30 ml of alcohol in 10 ml water. Bath temperature was 25°, air temperature 14°, pressure 717.5 mm, theoretical volume of hydrogen absorbed, H_0, was 252.8 ml. For the polarography, 1 ml of each sample was dissolved in 25 ml of the medium (0.1 N HCl in 96% alcohol). $\pi_{1/2}$ for maleic acid) 0.72 V, and for fumaric acid, 0.89 V. The concentration of each acid in the polarographed solution for sample No. 1, as sampled before hydrogenation, was equal to $0.005 = 500 \cdot 10^{-5}$ moles/liter. For convenience and for unity of concentration of the polarographed solutions, the concentration $1 \cdot 10^{-5}$ moles/liter was adopted. Then for the case investigated, the concentration of each acid, C, in relative units, was equal to 500.

During the course of hydrogenation, 12 samples were taken and polarographed. By measurement of the polarographic wave heights for both acids, their concentrations in each sample were determined, after which the reaction mixture composition following each consecutive state of hydrogenation, was calculated. The resulting data are given in Table 2.

TABLE 2

Sample No.	H_2 absorbed (in %)	Maleic acid		Fumaric acid		Composition of mixture (in %)		
		C	Saturation (in %)	C	saturation (in %)	maleic acid	fumaric acid	succinic acid
1	0	500	0	500	0	50.0	50.0	0
2	8.3	420	16.0	500	0	42.0	50.0	8.0
3	17.0	338	32.4	500	0	33.8	50.0	16.2
4	25.7	250	50.0	500	0	25.0	50.0	25.0
5	34.7	198	60.4	456	8.8	19.8	45.6	34.6
6	43.8	134	73.2	428	14.4	13.4	42.8	43.8
7	53.3	58	88.4	410	18.0	5.8	41.0	53.2
8	63.1	47	90.6	323	35.4	4.7	32.3	63.0
9	73.3	0	100	267	46.6	0	26.7	73.3
10	83.6	0	100	164	67.2	0	16.4	83.6
11	98.2	0	100	58	88.4	0	5.8	94.2
12	100.0	0	100	0	100	0	0	100

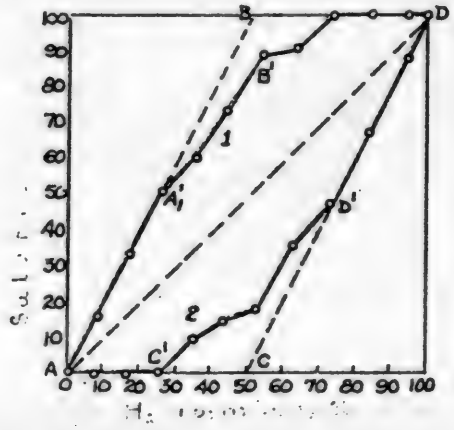

Fig. 1. Characteristics of selectivity of the hydrogenation process for a mixture of unsaturated compounds, using Pd and 25°. 1) Maleic acid; 2) fumaric acid. Explanations in the text.

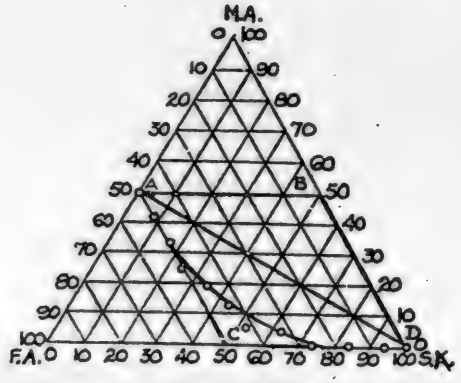

Fig. 2. Change in composition of the reaction mixture upon hydrogenation of the acids. M.A. = Maleic Acid; F.A. = Fumaric Acid; S.A. = Succinic Acid.

On the basis of the data in this Table, the curve (Fig. 1) was constructed. If the saturation process were completely unselective, then the saturation curve for each component of the mixture should coincide with the diagonal, AD. With completely selective saturation, for example of maleic acid, its saturation should proceed along the broken

line, ABD, and fumaric along the line ACD. Actually, the saturation curves showed certain deviations from the absolute selectivity.

Of special interest in connection with this fact is the nature of the degree of selectivity of the process.

A method for relating the content of saturated fatty acids in a fat with the iodine number [5] is well known, or a similar method for combining the iodine and thiocyanogen numbers for a fat, which have been applied to fats.

The A. A. Zinovyev method is of considerable interest, according to which the degree of selectivity is characterized by the ratio of the constants for the rate of saturation of both components of the mixture: $K=\frac{K_1}{K_2}$ [6]. However, it would have been more convenient, in the author's opinion to select the value, $1-K$, to characterize the process. This value for a completely selective process is equal to 1, if completely unselective, 0, and for any other it acquires a value lying between 0 and 1, and therefore, is closer to 1 the more selective the process.

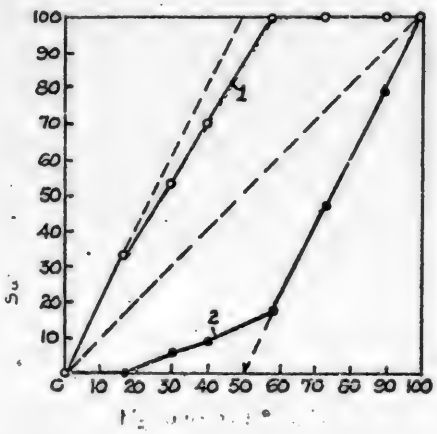

Fig. 3. Characterization of the degree of selectivity of the hydrogenation process for unsaturated acids, using Pd and at 40°. 1) Maleic acid; 2) fumaric acid. Explanation in the text.

Inasmuch as each pair of curves for unsaturated compounds is constructed analogously to the one presented in Fig. 1, for purposes of clarity, it is possible, therefore, to characterize the degree of selectivity by the area defined by the closed curve, AA'B'DD'C', and the area of the parallelogram, ABDC. Apparently, in a strictly selective process, when saturation of one of the components of the mixture takes place along the broken line, ABD, and the second component along the broken line, ACD, this ratio becomes equal to 1; in a completely unselective process, where both compounds become saturated along the straight line AD, the ratio and the degree of selectivity are equal to 0; in the remainder of cases the degree of selectivity lies between 0 and 1. In the particular case of fumaric and maleic acids, according to experimental data from the 104th experiment, the degree of selectivity was found to be equal to $S=\frac{41.05}{50}=0.821$, where 41.05 and 50 are the areas for the figure (in cm^2).

Measurement of the areas of the figures with their irregular shape, is accomplished by means of a planimeter. Without a planimeter, this problem can be solved by gravimetric procedure.

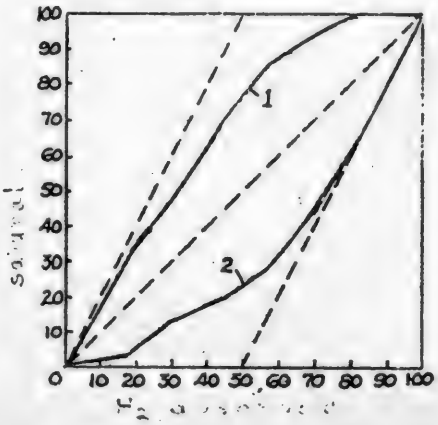

Fig. 4. Characterization of the degree of selectivity of the hydrogenation process for a mixture of unsaturated compounds, using Pt at 24°. 1) Maleic acid; 2) fumaric acid. Explanations in text.

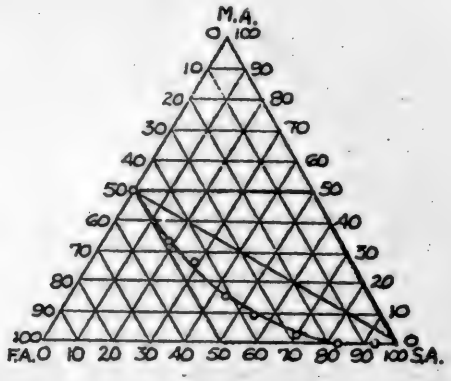

Fig. 5. Change in composition of the reaction mixture upon hydrogenation of the acids. F.A. = fumaric acid; M.A. = maleic acid; S.A. = succinic acid.

The change in composition of the reaction mixture, in agreement with the values in the last three columns of Table 2, is presented in a triangular coordinate system in Fig. 2. Point A corresponds to initial composition of the mixture; point D = the product from complete saturation. The transition from point A to point D can be realized by various routes: along the broken line, ABD, under the conditions of selective steric saturation, first with fumaric and then with maleic acid; along the broken line ACD with a strictly selective hydrogenation, first of maleic and then of fumaric; and along the straight line, AD, under conditions of completely unselective hydrogenation.

In the author's experiment, the points corresponding to composition of mixtures in a number of consecutive hydrogenation stages are distributed most closely to the broken line, ACD, on the AD curve. This indicates that the process proceeds with almost complete selectivity, maleic acid being saturated first, and then fumaric.

Similar experiments at 40° indicated a higher degree of selectivity, S = 0.874 (Fig. 3).

2. Hydrogenation of a Mixture of Maleic and Fumaric Acids with Platinum Catalyst

Experiment 158. A mixture of maleic and fumaric acids (in 1/200 mole portions), 210 mg of Al and 232 mg of Pt, 30 ml of alcohol in 10 ml of water. Bath temperature was 24°, air 11°, pressure 726.5 mm, theoretical hydrogen absorption, H_0, 243.8 ml. Results of the hydrogenation are given in the Figs. 4 and 5 curves. In this case, again maleic acid saturates predominately; however, the degree of selectivity was less than with hydrogenation in the presence of palladium catalyst (S = 0.686).

SUMMARY

1. The method of polarographic analysis has been used for the first time to investigate the hydrogenation process for mixtures of unsaturated organic compounds, which makes it possible to follow the course of the hydrogenation, and in particular the distribution of hydrogen between components in the mixture.

2. A method for quantitatively expressing selectivity of the hydrogenation process for binary mixtures by determining the ratio of figure area circumscribed by saturation curves for components of the mixture to the area corresponding to absolute selectivity of the process (S index) has been used.

3. It has been determined that for mixtures of geometrically-isomeric acids (maleic and fumaric) the first hydrogenates selectively for the most part, and selectivity is more pronounced when working with palladium catalyst than with platinum; however, in none of these cases does it bear an absolute character.

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